THE
LARYNGOSCOPE.

VOL. LII APRIL, 1942. No. 4

HISTAMINE IN THE TREATMENT OF NASAL ALLERGY (PERENNIAL AND SEASONAL ALLERGIC RHINITIS).*†

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Allergic diseases are defined as conditions in which the organism has become sensitized to substances which *per se* are innocuous, and in which the sensitized organism reacts with well defined symptoms on renewed contact with these substances. The application of this concept has led to the elaboration of valuable immunological methods in the diagnosis and treatment of those baffling conditions which were formerly known as idiosyncrasies. These methods have conclusively established the allergic etiology of the idiosyncrasies and have led to the development of specific desensitization therapy which has made possible the successful treatment of diseases which had resisted most previous therapeutic approaches. In view of these achievements it is understandable that the older workers in the field of allergy are well satisfied.

Theoretically, the immunological approach is ideal. All that one would have to do in a given case would be to determine the causative allergen or allergens and then to proceed either to eliminate them or to desensitize the patient with them. In practice, as most of us have learned to our sorrow, the situation is not so ideal, either from the diagnostic or from the therapeutic angle.

*Read at the meeting of the New York Academy of Medicine, Section on Otolaryngology, Jan. 21, 1942.

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Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, Feb. 25, 1942.

It is true that diligent search has led to the discovery of more and more allergens and to the introduction of more and more allergenic extracts into the treatment of allergic diseases, all of which must be very gratifying from the viewpoint of specific therapy. Some of us, however, have become perturbed by the ever-expanding multiplicity of allergens and the ensuing implications for specific treatment. An illustrative example of the consequences of this approach is the case of a person who was suffering from a severe food allergy and whose diet in the course of food elimination was finally restricted to four foodstuffs. As you will concede, this was a most trying situation for the patient. For the physician, the situation may also become very difficult if he has to use a very large number of substances for specific desensitization, and still possibly be in doubt whether he has really discovered all the offending allergens. As further development of allergy therapy along specific lines must of necessity lead to increasing complexity, we have aimed at nonspecific treatment; *i.e.*, we have striven toward reducing the treatment of allergic diseases to a common denominator.

Various attempts at nonspecific therapy have been made, the theoretically best-founded of which is based on the use of histamine. I have previously[1,2] discussed in detail the rationale of its use in allergic diseases. I shall therefore outline only briefly the underlying theory, which presupposes that the symptoms of experimental anaphylaxis and of clinical allergy are the symptoms of histamine poisoning. According to Dale's theory of anaphylaxis, the combining of antigen and antibody in sensitized tissues leads to cell lesion and the liberation of preformed histamine from these tissues. Thomas Lewis and his collaborators expanded this theory to explain allergic reactions in humans, and today it has been accepted by many that the symptoms of atopic as well as of physical allergy are due to the liberation of preformed histamine from the shock organs of allergic persons. Furthermore, it has been shown in experimental animals and in normal and allergic humans that it is possible to induce a tolerance to histamine.

These findings would explain why the symptoms of allergic conditions are independent of the nature of the causative allergen, and dependent only on the reaction of the shock organ. They further form the theoretical basis for the use

of histamine in allergic diseases. It is obvious that if histamine could be used successfully in the treatment of allergic conditions, it would reduce their therapy to a common denominator. It would obviate the necessity of using a different agent for each allergy and would thus make for much simplification. Its use would be especially indicated in cases of multiple sensitiveness and also in those cases which might be on an allergic basis in spite of the fact that the causative allergen could not be elicited. Histamine treatment should also be successful in physical allergy.

In 1924, Ramirez and St. George first reported the use of histamine in the treatment of bronchial asthma. In the 15 years which followed their important publication, up to 1939, there appeared in the American literature only four papers on the histamine therapy of allergic conditions. During this time workers in France had become interested in the subject and a few reports had also appeared in England and Germany. All these authors were impressed by their results. In the past two years there have appeared in this country further publications on histamine therapy in allergy.[3,4,5]

For five years we have been using histamine extensively in various forms of allergy in my clinic at Lenox Hill Hospital. Our therapeutic results have been gratifying, and I appreciate the opportunity of presenting to you our experiences with this form of treatment in nasal allergy. My collaborators and I are internists, and most of the cases we are presenting have been examined and diagnosed by our otolaryngologists, without whose help this investigation would not have been possible.

Nasal manifestations characterized symptomatically by itching, sneezing, nasal obstruction and watery discharge, and pathologically by turbinal pallor and edema, and which are not caused by infection, are frequently due to allergic hypersensitiveness. Thus it has been shown that practically all cases of seasonal rhinitis are caused by hypersensitiveness to pollen, and that a large percentage of cases of perennial rhinitis are due to other inhalants, such as danders and dusts, and, to a lesser degree, to foods and bacteria. Following an accepted terminology, we are designating these conditions as seasonal allergic rhinitis or hay fever, and as perennial allergic rhinitis. The term "vasomotor rhinitis" would then be reserved for turbinal edema of noninfectious

and nonallergic origin. Hansel,[6] however, raises the question whether there really is a "so-called nonallergic type of vasomotor rhinitis." He believes "that all cases of vasomotor rhinitis are of allergic origin in spite of negative skin tests, and that in these particular cases the nasal mucous membrane is hypersensitive and the skin is not." If Hansel's conception is correct, this type of case would be very appropriate for histamine therapy.

We have treated patients suffering from perennial as well as from seasonal allergic rhinitis with histamine. The developed technique differs somewhat in the two types and they are therefore presented individually. The histamine used was histamine phosphate U.S.P., which, chemically, is histamine diphosphate and which contains 36 per cent histamine base. Other authors have used histamine dichloride, which contains 75 per cent histamine base. It is important to consider these relationships.

PERENNIAL ALLERGIC RHINITIS.

In this group there were 41 patients, of whom 13 were males and 28 females. Their ages ranged from 7 to 57 years. Twenty-seven patients had nasal manifestations only, the others suffering also from further manifestations of allergy. On rhinoscopic examination, 19 patients showed a typical pale, swollen, boggy nasal mucosa; in eight patients who had been examined on the outside, we were not able to get the results of the otolaryngological examination. The majority of the patients showed positive skin reactions to one or more allergens. These allergens were eliminated if possible, and histamine therapy was instituted only if the elimination did not lead to the desired therapeutic result.

The histamine was given by subcutaneous injection. The initial dose was 0.01 to 0.1 gamma (1 gamma is 1/1000 mg.). The highest dose in perennial rhinitis was 100 gamma. We believe that these small doses are of utmost importance. According to our opinion, the earlier workers used too large amounts of histamine. The injections are increased each time by 50 per cent, if well tolerated, and in the beginning they are given two to three times a week. They are later spaced at approximately five-, seven-, 10-, 14- and 21-day intervals. The greatest therapeutic difficulty lies in the impossibility of

developing a hard and fast schedule of dosage. The rapidity with which the doses are increased and the spacing of the injections will depend on the patient's tolerance and the results achieved. We have been impressed by the fact that the therapeutic effect achieved with small amounts of histamine is frequently much better than that achieved with higher doses. During the course of treatment we have repeatedly seen a patient's condition deteriorate after initial improvement. On analyzing our therapeutic procedure, we came to the conclusion that the patient was being overdosed; on subsequent reduction of the doses the patient again improved. Some of our best therapeutic results were in fact achieved with doses not exceeding 3 gamma. If this should appear like black magic, I should like to recall that the uterine strip of normal guinea pigs will contract maximally in a histamine solution of 1:100,000,000 and, furthermore, that we have observed severe headache lasting for 18 hours after an injection of 0.33 gamma.

As in specific desensitization, histamine injections should be continued over a considerable period of time at two-to three-week intervals, especially if the therapeutic results are good. These recommendations are purely empirical, as we do not know by what mechanism tolerance to histamine is produced.

The precautions to be taken are the same as in specific desensitization. Care must be taken not to inject the histamine into a venule or capillary; adrenalin and a tourniquet should always be on hand; and the patient should be observed for 10 to 15 minutes after the injection. However, we feel that histamine treatment causes less severe and less frequent systemic reactions than specific desensitization. In the course of several thousand injections of histamine, we have encountered systemic reactions in a few instances only. They consisted of headache, mild angioneurotic edema, and in one instance in a severe attack of urticaria. The amounts of histamine that sufficed to bring on these reactions were very small; they varied from 0.33 to 1.0 gamma.

In evaluating our therapeutic results we have designated as "good" those cases in which marked alleviation of the symptoms was achieved; as "fair" those in which a moderate degree of improvement was effected, and as "poor" those in which there was little or no improvement.

As stated above, 41 cases of perennial rhinitis were treated. In 25 cases the result was good, in 10 fair and in six poor. Fifteen of the 41 cases were severe; in 10 of these a good therapeutic result was achieved.

The following are the histories of two successfully treated patients:

A. B., school girl, age 15 years, was referred to us from the otolaryngologic clinic. She had been suffering for four years from nasal obstruction, occasional paroxysms of sneezing, dyspnea and itching of the eyes. These symptoms persisted the year round. Her nasal membranes were pale and the inferior turbinates were greatly swollen. There was no evidence of involvement of the sinuses. The medical examination was essentially negative. Skin tests were markedly positive for house dust, cat dander, dog dander, rabbit dander, feathers, sheep wool and ragweed pollen.

Histamine treatment was started with 0.03 gamma on March 27, 1940. There was noticeable improvement of the patient's condition by the middle of May, at which time she had received 11 injections; the highest dose then was 1.5 gamma. Treatment was continued during the next months with further alleviation of the symptoms. The patient was in the country for a few days at the beginning of July, during which time she had considerable sneezing. The symptoms subsided after her return to the city. She received the last (twenty-sixth) injection of histamine, 10 gamma, on Aug. 5. The patient continued to feel well until the beginning of September, at which time she had mild ocular, nasal and pulmonary symptoms which lasted for two weeks. These symptoms were undoubtedly due to her ragweed sensitivity. The patient should have received histamine injections during the ragweed pollinating season, and today we would treat her that way.

During the course of the treatment the patient showed repeated systemic reactions to histamine. After the second injection, which consisted of 0.1 gamma, there was a marked increase of the sneezing and also edema of the eyelids and itching and watering of the eyes. After the sixteenth injection (10 gamma) the patient developed an itching eruption about the size of a silver dollar on the face. Two hours after the eighteenth injection (13 gamma) she developed urticaria

of the face, neck, and arms, which persisted for one week. Her nasal symptoms were very much improved. Several hours after the twentieth injection, on June 14, she again had an itching eruption on the face. This injection had been reduced to 7 gamma. After the following injection she again developed an urticarial eruption of the face. In the beginning of October there was a marked flare-up of the patient's rhinitis and it was decided to start the patient again on histamine. Immediately after the third injection (0.3 gamma) the patient noticed itching of the skin of the face and an eruption on the face and neck, and slight swelling of the eyelids. We felt that under the circumstances histamine treatment should be discontinued. The patient was again seen in February and in March, 1941, one year after her first visit to the clinic. She was feeling well and reported that she had had only very mild nasal symptoms during the winter. We then lost track of the patient.

F. L., baker, age 36 years, had been suffering for three years from severe attacks of paroxysmal sneezing, accompanied by profuse watery nasal discharge. His symptoms occurred only in the bake shop and only when the patient worked with wheat flour. The attacks commenced one to two hours after he went into the shop and lasted for many hours.

The patient's personal and family histories were not contributory. Intradermal skin testing with wheat extract gave a strongly positive reaction. Histamine treatment was started with 0.1 gamma on Feb. 21, 1938. Decided improvement was noted after the eleventh injection, which amounted to 3 gamma. The improvement continued and the patient was able to carry on his work during April, May and June without any symptoms of rhinitis. He was getting histamine injections during this time. The last (twenty-fourth) injection of 40 gamma was given on July 6. During the summer the patient had only very mild and infrequent symptoms of rhinitis in spite of the fact that he was working during this time. He came back to the clinic on Sept. 21, 1938, as he had been sneezing more frequently for the past week. He was given four injections of histamine, which helped him materially. On July 28, 1939, the patient reported that he had been working steadily with wheat flour since Nov. 1, 1938, and that he had had no symptoms of rhinitis. We have not heard from the patient since that time.

SEASONAL ALLERGIC RHINITIS.

From a theoretical point of view, we were especially interested in ascertaining the effect of histamine therapy in seasonal allergic rhinitis. Our therapeutic results in this form of nasal allergy, as well as in perennial allergic rhinitis and asthma, and also the experience of Porch,[4] clearly refute the contentions of Alexander.[3] In a paper in which he discusses the use of histamine in allergic diseases, he states that the conditions in which this therapy is successful "differ from asthma, hay fever and atopic eczema in that no extrinsic allergens as pollens, foods, etc., are usually identified." He goes on to say that "chronic urticaria and angioneurotic edema, types of 'physical allergy,' headaches and Ménière's syndrome are the only manifestations associated with allergy in which histamine has been used with any measure of success."

Hay fever is an unquestionable atopic allergy in which the causative allergen is usually readily identified and which presents a clear-cut clinical picture. We feel that the successful use of histamine in the treatment of hay fever would constitute further evidence of the correctness of the histamine theory of allergy.

In this investigation we treated 90 cases of pollinosis with injections of histamine phosphate during 1938, 1939 and 1940. These 90 "cases" occurred in 71 patients, 14 of whom were treated during two or three consecutive years. In 72 cases the symptoms were due to ragweed pollen; in 15 to grass pollen; in three to tree pollen.

For the treatment of uncomplicated cases of tree, grass or ragweed hay fever we have developed the following routine: Treatment is started eight to 10 weeks before the onset of the pollinating season. During the first month the injections are given twice a week, thereafter once a week, and are continued at this interval until the end of the pollinating season. According to this schedule, approximately 14 injections are given prior to, and four to six injections during the pollinating season, a total of 18 to 20 injections.

The initial dose is 1 gamma (0.001 mg.) if the patient (adult) shows no allergic symptoms at the time treatment is started. If the injections are well tolerated, subsequent doses

are 2, 4, 8, 15, 30, 50 and 75 gamma. These eight doses are given during the first month of treatment at about four-day intervals. The ninth to fourteenth doses are 100 gamma each and are given at an interval of one week. This leads up to the onset of the pollinating season, at which time the dose is reduced to 30 gamma and (if well tolerated) is continued at this height at weekly intervals to the end of the pollinating season. The total dosage according to this schedule amounts to 965 gamma. In children we begin with 0.1 gamma, increase the dosage by only 50 per cent and usually do not go beyond 50 gamma.

In the evaluation of our therapeutic results in hay fever we have again designated as "good" those cases in which marked or complete alleviation of the symptoms was achieved; as "fair" those in which moderate improvement was effected; and as "poor" those in which no appreciable relief was experienced.

Of the 72 ragweed cases, 24 were considered severe; in seven of these a good and in nine a fair result was achieved. Forty-eight ragweed cases were classed as moderate; in 19 the result was good and in 13 fair. These figures show that in 66 per cent of the severe cases a good or fair therapeutic result was obtained, the same percentage as in the moderate cases. Fifteen cases of grass hay fever were treated; four were severe and 11 moderate; in nine a good and in six a fair result was achieved. The same satisfactory results were obtained in tree pollinosis.

The reported results in simple, uncomplicated cases of pollinosis show conclusively that hay fever, an atopic allergy, can be successfully treated with injections of histamine. This finding is further evidence of the correctness of the histamine theory of allergic conditions. The percentage of good therapeutic results achieved with histamine in hay fever is up to now not so high as that achieved with specific desensitization. This may well be due to imperfect knowledge of the optimal therapeutic conditions. We believe that further experimentation will lead to improved results.

At the present time we do not recommend histamine treatment in simple, uncomplicated cases of pollinosis. However, its use is indicated in those cases of hay fever in which spe-

cific desensitization treatment has not been successful, or in which it has caused severe reactions. It is further indicated in cases of pollinosis in which there are also perennial manifestations of allergy such as asthma or perennial rhinitis.

CONCLUSIONS.

1. Although specific treatment of allergic diseases has been a great step forward, it has not solved all involved therapeutic problems.

2. The use of histamine in the treatment of allergic conditions appears to be theoretically sound, as this substance is very probably responsible for the symptoms of allergy, and as it is possible to induce a tolerance to histamine.

3. We have been able to treat successfully patients suffering from nasal and other forms of allergy by repeated subcutaneous injections of histamine.

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DISCUSSION.

DR. ARTHUR J. CRACOVANER: Dr. Farmer's presentation is one of exceptional importance to otolaryngologists. We have all seen patients with allergic manifestations come to our offices in increasing numbers. We have all recognized these manifestations and then requested a consultation with an allergist, who in turn performs the usual great number of tests in order to determine to which particular allergen the patient is hypersensitive. There are times when one or several substances give positive reactions. When such substances are eliminated or when the patient is desensitized by a series of injections, marked improvement is frequently noted. However, in a great many instances the patient is hypersensitive to so many substances that to eliminate them all is exceedingly difficult. Then again, in a good percentage of cases no specific hypersensitivity is found, or even after treatment the result is not entirely satisfactory. In such cases it would be a great boon to our patients, as well

as to ourselves, if a nonspecific therapy such as histamine therapy could be found to give either complete or partial relief. One would be able to dispense with performing so many tests on a patient, for the number of allergens is ever increasing and it is an ordeal that so frequently gives negative or discouraging findings.

According to Dr. Farmer's report up to the present time, histamine therapy is more than promising. I have had the good fortune to see and follow a great many of the cases in Dr. Farmer's series and have been amazed at the good results that he has obtained. It is just the kind of case in which the patient is hypersensitive to a great many substances that this nonspecific therapy is valuable. I have also seen a few so-called "physical allergies" markedly improved or completely kept under control by histamine injections; the type of case, for instance, that has nasal symptoms which are brought on by changes of temperature and that complains of cold or chilly sensations at the same time. Certainly there is no specific therapy for a sensitivity to heat and cold. Yet, under this treatment, as a patient recently told me, they lose that feeling of chilliness with changes of temperature. This is one of the instances where nonspecific therapy is especially indicated and effective.

Results obtained in pollen hypersensitivity are interesting even though they do not equal the benefit that is reported in specific therapy. However, we all have seen instances where the patient has not only a pollen hypersensitivity but also reacts to other allergens. Then, too, there are cases that are not improved by specific pollen treatment. These are certainly cases that should receive the benefit of histamine therapy.

Dr. Farmer has described the allergic nose as the pale, boggy, white, swollen, moist mucosa. This is the type of allergic reaction in the nose that one commonly sees. However, we frequently see a red, swollen mucosa in allergic cases and in some instances this redness is not due to infection. Sometimes endocrine disturbances have this type of influence on the nasal mucous membrane. Such a case is frequently called vasomotor rhinitis. It is often alleviated by the proper endocrine therapy. It is interesting to note that a few of the patients treated with histamine by Dr. Farmer and known to me to be cases with endocrine disturbances were definitely benefited by histamine therapy. I wonder if Dr. Farmer has an explanation for this, or is it a problem that must be worked out in the future?

I feel histamine as a nonspecific therapy in allergic and vasomotor rhinitis has a definite place in the future of nasal treatment. I believe Dr. Farmer is to be complimented on his diligent and careful work on this subject, and we are grateful for this presentation to us.

Dr. Hyman John Rubenstein (by invitation): I had occasion to hear Dr. Farmer's last presentation before the Section of Medicine, and obtained the details of his technique. I have seen a good many patients coming in with the problem of vasomotor rhinitis complicating sinus infection, and I took the opportunity of working up in great detail a series of more than 100 cases. We use intradermal desensitization, beginning with a dose of one-hundredth of a gamma and going up to 200 or 300 gamma. In an experience of 200 cases, 75 per cent of them vasomotor rhinitis, and most of them with multiple sensitivities, particularly to dust and physical allergens, I can state that from the point of view of the results obtained, most of those with physical allergies were completely relieved. Among those who had a vasomotor rhinitis due to food or dust, I doubt that more than 2 per cent to 3 per cent were helped. Some, where the primary sensitivity was due to dust, were helped in very slight degree. There were some people among the series who had such allergic manifestations as Ménière's syndrome, and by beginning with a very small dose and going up, those patients, numbering five, were completely relieved. In my experience, if the patient presents a picture of physical allergy, his chances of relief from this treatment are up to 95 per cent but, unfortunately, the results in vasomotor rhinitis are bad.

Dr. Emil Glas (by invitation): I have tried all the suggested treatments during past years — specific desensitization, nonspecific treatment, iontophore-

sis with zinc sulphate, trichloracetic acid therapy (which I introduced), bismuth injections, histaminase injections, intravenous calcium injections, caustic applications to the nasal mucosae, and five years ago I first used the histamine treatment in cases of allergic rhinitis (vasomotor or nervous rhinitis) by iontophoresis through the nasal mucosa. The best results were obtained in those cases where specific desensitization was possible. All methods had good results in certain cases and failure in others. Histamine iontophoresis in increasing doses, beginning with a solution of 1:2,000, had excellent results in some instances. There was a slight reaction at times, but never bad side effects. I think the reason this method of application had good results is because of the direct contact of the introduced histamine with the shock tissue of the nose. Horton, of the Mayo Clinic, has used injections of histamine in the treatment of certain forms of headache with good results. His method seems to be the same as that of Dr. Farmer.

I would suggest that exaggeration of the value of histamine treatment should be avoided. There is no universal remedy for vasomotor rhinitis.

DR. LAURENCE FARMER: Dr. Rubenstein's report interested me very much. I cannot explain why our results are better than his, unless it is due to the fact that we have been using this method for five years and he for only one. Another explanation may be that his doses were too large. I recently had occasion to see a number of patients who for quite a long time could not tolerate more than 0.02 or 0.03 gamma of histamine. We have watched these cases very carefully and have found that if they were kept on the same dose for a considerable period of time improvement was achieved, whereas if the doses were increased the patients would relapse. As histamine is the substance which causes the symptoms, too large amounts can aggravate them.

I was interested in Dr. Rubeinstein's good results in physical allergy. This alone would make histamine therapy very worth while; however, I know that histamine also helps in atopic allergy. Hay fever unquestionably is an atopic allergy, and it is unquestionable that it can be alleviated by histamine therapy. The degree of alleviation has no bearing on the principle involved.

In answer to Dr. Glas, I must say that I have had no personal experience with the local application of histamine by ionization. Our objection to this method is that the dosage is hard to determine. One can take a known amount of the drug but one does not know how much the patient is resorbing. I feel convinced that good results can be obtained by ionization; this can be expected on the basis of the work of Thomas Lewis. Lewis punctured histamine into skin and found that these areas eventually became nonresponsive. I believe that there is a difference between histamine tolerance and histamine nonresponsiveness, but I cannot now go into that question. As far as therapy goes, I could see that the results, especially in hay fever, would be the same irrespective of whether the membrane has become nonresponsive to or tolerant of histamine.

Dr. Glas spoke of the use of histamine as "Farmer's method." I am sorry to say that it is not my child; I am only its foster-father.

950 Park Avenue.

OSTEOMYELITIS OF THE FRONTAL BONE.*

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A perusal of the recent literature impresses one with the rarity of osteomyelitis of the frontal bone, especially when one considers the frequency of suppurative disease of the various accessory paranasal sinuses. A. E. Bulson, Jr.,[1] was able to find only 55 cases in a complete review of the literature for 30 years previous to 1925. Furstenburg[2] found only 73 cases of osteomyelitis of the cranial vault up to that date. In his article he reports 14 cases which he has personally observed at the University Hospital. In this group there were eight recoveries and six deaths.

Etiology and Bacteriology: Frontal sinusitis is the most common etiological cause of osteomyelitis of the frontal bone, this complication occurring spontaneously or postoperatively. The suppurative disease of the underlying sinus may be acute, chronic or an acute flare-up of a chronic infection. Trauma, too, may be the exciting cause, even though there is no evidence of a previous suppurative involvement of the underlying cranial sinus.

The staphylococcus is the organism most frequently isolated on culture, though no mention is made of bacteriology in numerous articles. Bulson[1] reports as follows:

Total cases 20	Deaths 9	Mortality	45%
Pneumococcus 1	0		0
Streptococcus 5	5		100%
Staph. aureus 14	3		21%

A few authors report more than one organism isolated on the culture; Watkyn-Thomas and McKenzie[3] isolated streptococci and a coliform bacillus. They state: "Both of these organisms may be a contamination or possibly the osteomyelitis may be due to the two organisms attacking together, one reducing the resistance of the bone to the action of the other." The Mayo Clinic has isolated an anerobic streptococcus by culturing the bone in dextrose brain broth. They feel

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Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, Aug. 31, 1941.

this is the causative organism, and that the staphylococcus, streptococcus and pneumococcus are secondary invaders.

Types: Three clinical types of osteomyelitis of the frontal bone are recognized at the Mayo Clinic, and discussed by Williams and Heilman.[4] They describe the localizing, the fulminating and the spreading types, each of which may merge into the other. "The fulminating type frequently follows swimming, and is characterized by intense pain in the frontal region, generalized headache, high fever, rapidly spreading edema and a tendency to spread early to the arachnoid process and cranial sinuses. In the localizing type, after an initial advance, the process becomes completely isolated by reactive barriers, with eventual marginal sclerosis of bone. In the spreading type the resistance is sufficient to prevent rapid advance but there is no tendency to complete localization."

Pathology: The pathology and the mode of spread of infection in osteomyelitis secondary to disease of the frontal sinus has been outlined by Furstenburg.[5] The infection may spread by two methods: *1.* By direct extension from the frontal sinus into the adjacent diploe; *2.* by the hematogenous route, the thrombophlebitis of the diploic veins penetrates the cerebral wall of the frontal sinus, spreads through the diploic system of vessels within the dura mater, and an exudate forms between dura and skull. As a result the blood supply of the bones is cut off, which tends to deprive them of nutrition and lays them open to widespread infection from the sinus.

Treatment: The treatment of osteomyelitis is directed: *1.* to general supportive measures to increase the resistance of the patient; and *2.* local treatment to eradicate all diseased bone and tissue. Two schools put forward their arguments in local treatment for: *1.* conservative; and *2.* radical surgery. Blair and Brown[6] strongly advocate conservative treatment. They advise early drainage, allowing the virulence of the infection to subside; the removal of sequestra as they separate; and the later removal of the edges of all live bone that overhangs, so that soft tissue may drop in and fill the defects. Furstenburg,[5] Mosher and Judd[7] advise wide radical resection of both the inner and outer tables of the skull, well beyond the limits of the disease, so as to include the area of thrombosed diploic veins.

Review of 10 Cases: Briefly, we wish to review 10 consecutive cases of osteomyelitis of the frontal bone, taken from

our records, all of which occurred before the advent of effective chemotherapy. These 10 cases of osteomyelitis were all of the localizing type, and the conservative type of treatment was carried out on all of them. A simple incision was made over the area of fluctuation and a drainage tube inserted. The acute infection was allowed to subside and sequestra were removed as they separated. Vaccines were given to two patients preoperatively, and transfusions administered to several patients before operation. When the general condition of the patient warranted an operation, and the local infection appeared to have subsided, the frontal sinus was opened externally, diseased bone, pus and infected mucous membrane were removed, and drainage provided into the nose. Our mortality was two cases, or 20 per cent — one patient had an actinomycosis infection and died of a brain abscess, from which this fungus was isolated at autopsy; the second patient had previous operations on the frontal, ethmoid and maxillary sinuses, and the osteomyelitis was secondary to a second frontal operation. This patient developed bilateral frontal and parietal abscesses, which were incised and drained, but patient succumbed to bronchopneumonia and leptomenigitis.

Onset:	No.	Well	Death	Mortality
Spontaneous	7	6	1	14%
Postoperative	1	0	1	100%
Traumatic	2	2	0	0
Cultures:				
Staphylococcus	5	4	1	20%
Pneumococcus IV	1	1	0	0
Nonhem. strep.	1	1	0	0
Actinomycosis	1	0	1	100%
No culture	2	2	0	0

The majority of our patients were under 30 years of age; four between 10 and 15 years of age; two between the ages of 20 and 30 years; two between 30 and 40 years; one 58 years of age; and one 65 years of age. In this small series, six, or 60 per cent, of our cases occurred under 30 years of age — nine patients were males and only one a female.

In six of these patients the posterior plate of the frontal sinus had been eroded or was a sequestrum, and the dura was exposed. In only three of these six patients did a frontal

lobe abscess develop, and two of these recovered after drainage of the abscess. One of the patients who recovered, a boy, age 15 years, with a frontal lobe brain abscess, became a mental patient.

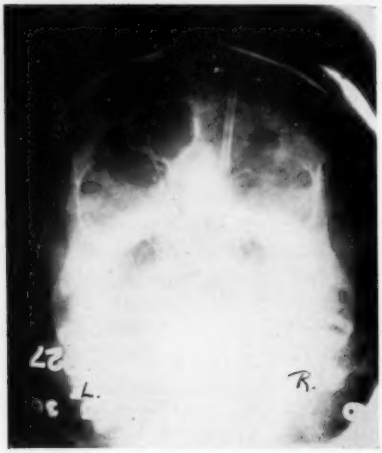

Fig. 1. Case 1: X-ray showing infection of right frontal sinus and osteomyelitis of frontal bone. A drainage tube is present in frontal sinus.

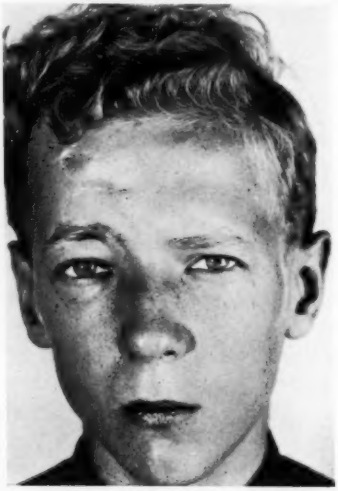

Fig. 2. Case 1: Postoperative photograph of patient. Very slight deformity is noticeable.

CASE REPORTS.

Case1: F. K., No. 222,927, age 13 years., M. W. Wassermann negative, Sept. 16, 1935.

C. C.: Swelling of right upper eyelid.

P. I.: Following a tonsillectomy and adenoidectomy four days previously, patient developed a swelling of the right upper eyelid.

P. E.: A red, soft, nonfluctuant swelling of right upper eyelid was noted. There was pus in the right nostril, which appeared to come from the right nasofrontal duct. The right middle turbinate was congested. Right frontal sinus was dark on transillumination and tender on palpation. General physical examination was negative except for foul dis-

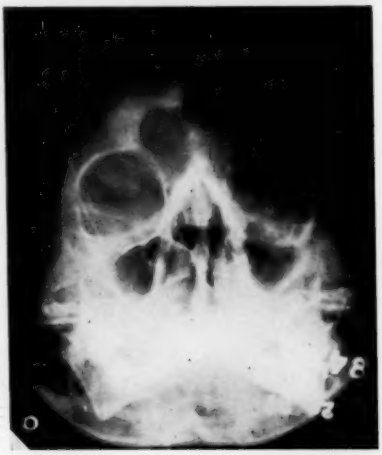

Fig. 3. Case 2: X-ray showing infection of right frontal sinus and surrounding osteomyelitis.

charge right external auditory canal, absent drum, granulations in middle ear. X-ray showed infection of the right mastoid.

The differential diagnosis was between a beginning osteomyelitis of the right frontal sinus and a cavernous sinus thrombosis.

Sept. 17, 1935: Intranasal ethmoid operation with opening into frontal. Considerable pus from frontal. Culture: Staphylococcus pyogenes aureus.

Sept. 19, 1935: Swelling had spread over right frontal region. Swelling of right upper eyelid incised and about three drams of thick, yellow pus evacuated.

Sept. 23, 1935: Incision and drainage, abscess right frontal region — thick pus — no perforation into frontal could be felt. Given blood transfusion.

Nov. 1, 1935: Incision and drainage, right frontal abscess. Sequestrum of bone removed and opening found into right frontal. Drainage tube inserted. Frequent irrigations of frontal sinus with normal saline solu-

tion. On three occasions small sequestra of bone were removed. No headache, no nausea or vomiting.

Dec. 1, 1935: Began a series of staph. toxoid injections.

Feb. 19, 1936: External frontal operation with removal of anterior wall and floor of frontal sinus and collapse of the sinus. A few sequestra were removed from anterior wall and floor of sinus. At upper border a sequestrum of posterior plate was removed and dura was exposed. The frontal sinus contained pus and thick polypoid mucous membrane.

Patient made an uneventful recovery — right radical mastoid, March 19, 1936. This boy is alive and well, five years after operation, with no recurrence of the osteomyelitis.

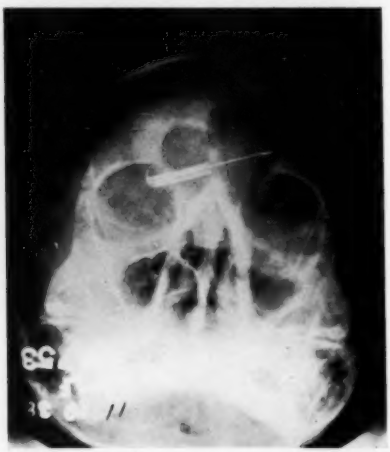

Fig. 4. Case 2: After incision of orbital abscess. A drainage tube is present in right frontal sinus, and a probe projects through tube into left frontal sinus.

Case 2: M. H., No. 284,753, F. W., age 65 years. Wassermann negative.

C. C.: Swelling of left eye. First seen Nov. 28, 1938.

P. I.: July, 1938, had pneumonia with good recovery. Two months later developed a head cold which cleared up. About six weeks previous to admission patient developed redness and swelling of right eyelid which subsided, and then redness and swelling of left eyelid developed which persisted. For the past month has experienced severe frontal headaches, more marked on the right side. Has never had nasal obstruction or discharge, but lately had a series of nasal treatments without relief. Two weeks before admission had severe chills.

P. E.: No nasal congestion or discharge. No hypertrophy of turbinates. Slight redness of right upper and lower eyelids. Marked redness of left upper and lower eyelids with edema of left upper eyelid. Firm, very tender, fluctuant swelling over anterior surface and floor of left frontal at inner canthus.

X-ray: Fig. 3 shows infiltration of frontal bone around frontal sinus on right side. Appears to be some erosion of frontal plates, with a soft

tissue abscess a question. There appears to be considerable infiltration of the frontal bone for about 5 or 6 cm. upward from upper margin of frontal sinus.

Nov. 29, 1938: Incision through floor of frontal — frank pus evacuated. Tube inserted. Culture: Nonhemolytic strep.

Feb. 10, 1939: Bilateral ethmoidectomy.

Feb. 14, 1939: Bilateral external frontal operation. Loss of bone of almost the entire anterior wall of left frontal sinus, and loss of floor and

Fig. 5. Photograph of patient, age 65 years. Note abscess of right orbit and frontal region.

Fig. 6. Case 2: Postoperative appearance.

nasal process left. The anterior wall of the right frontal sinus was soft and showed evidence of osteomyelitis. The right frontal was filled with pus. The posterior plate on the right side was eroded and the dura exposed by disease.

Following operation it was discovered that patient had a blood sugar of 236. Put on a diabetic diet and insulin.

Uneventful recovery.

Comment: Although all the patients in this small series of cases have been treated conservatively, with a rather low mortality for this dreaded complication of frontal sinus infection, we are not reluctant, if called upon, to do extensive radical surgery. It is our feeling that each patient should be treated as an individual, and clinical judgment should dictate the type of treatment and the extent of surgery. In all types of osteomyelitis of the frontal bone, conservative treatment may with safety be tried for several days. In the localizing type, conservative treatment and conservative

surgery in our experience have given very excellent results, a low mortality and a minimal deformity. In the spreading type of infection, after an interval of conservative treatment, in an effort to localize the infection, radical surgery should be resorted to, if the infection tends to progress. The radical surgery should include removal of both the inner and outer plates of the frontal, well beyond the limits of infection. In the acute fulminating type of osteomyelitis, simple drainage of pus through a small trephine opening near the inner angle of the brow, and simple measures to build up the resistance of the patient should be advocated in an attempt to localize the infection. If the infection shows evidence of subsiding, it may be treated as a spreading or a localizing type and adequate surgery done to clear out all the infection. If the infection shows no tendency to localize, and the patient is unable to build up reactive barriers, further surgical interference usually proves futile.

Conclusion: The occurrence of osteomyelitis in cases of frontal sinus infection is still a problem. It is a serious complication, and much more so when it occurs postoperatively. Perhaps chemotherapy may lessen the frequency of its occurrence and prove of value, not only in the treatment but also in reducing the incidence.

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THE "ILLUSION OF LOUDNESS" OF TINNITUS— ITS ETIOLOGY AND TREATMENT.*

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One type of tinnitus produces no illusion because it is in fact a real sound resulting from actual mechanical vibrations. This type of tinnitus I call vibratory tinnitus. It is just as real as the sound heard when bells ring, buzzers buzz or tuning forks vibrate, when some of the frequencies in environmental noise are accentuated by resonators like cockle shells. Vibratory tinnitus, if loud enough, can be (and frequently is) heard by the examiner. This is an infallible test of its vibratory origin, as is the production of beats when a nearly identical frequency to the tinnitus is applied to an ear harboring a tonal tinnitus.

Since vibratory tinnitus is a real sound, its loudness is real; it is not an illusion. It is an actual sensation depending upon the amount of vibratory disturbance at its source and the impedance in the media traversed to reach the inner ear. The sensation of loudness or vibratory tinnitus is, of course, also dependent upon the health of the auditory apparatus in the ear, its pathways in the brain stem, and the individual sensitiveness to the vibrations.

Conduction deafness will generally favor a louder reception of vibratory tinnitus than nerve deafness because it excludes environmental masking sounds by lowering air conduction, but does not lower the bone conduction; in fact, it often appears to increase bone conduction. Conduction deafness places the sufferer in a quieter place than if he had no deafness, no matter where he happens to be.

Nerve deafness does not cut down loud extraneous sounds to the same extent as conduction deafness because of the recruitment phenomenon which is always present with nerve deafness and which accounts for the fact that very loud sounds may be heard by people with pure nerve deafness near normal loudness. In the presence of pure nerve deafness,

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*Read at the meeting of the New York Academy of Medicine, Section on Otolaryngology, April 16, 1941.

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, June 25, 1941.

vibratory tinnitus being in fact an environmental noise is heard in the same way as environmental noise. Vibratory tinnitus, like environmental noise, does not originate within the inner ear or from the auditory nerve and, therefore, may be mechanically impeded or aided in reaching the inner ear. When environmental noise and tinnitus occur coincidentally, one or the other may predominate or entirely mask the other. This largely depends upon which is the louder and also upon their frequency content.

Vibratory tinnitus usually comes to the ear through the solid and liquid media of the tissues rather than through the gaseous elements (the air), and may, therefore, be considered a bone conduction tinnitus. It is difficult to think of it as not always being a bone or tissue conduction tinnitus because, even though it originates in intratympanic, tubal, nasopharyngeal or vascular structures, the vibrations are carried to the cochlea with only incidental vibration of the air in the external meatus or middle ear. Vibratory tinnitus, like all other actual sound, is always easily masked by sounds near to and below it in frequency.

The more common types of vibratory head noises arise from contractions of the intratympanic and tubal muscles, extracranial aneurysms, arterial or arteriovenous aneurysmal angiomas, bruits in the jugular bulb or vein, other hemic murmurs, clicks and squeaks about the jaw joints, spasms of facial and neck muscles, bubbles in the Eustachian tubes, and various sounds from the respiratory and gastrointestinal tracts. It is believed that vascular brain tumors and intracranial aneurysms seldom cause vibratory tinnitus, but they may initiate nonvibratory tinnitus; in fact, tinnitus may be the first symptom of their presence.

The frequency content of vibratory tinnitus may be made up of a broad band of frequencies (noise), narrow bands of frequencies, or be of tonal quality. If tonal, the fundamental frequency will be low — usually well below 256 d.v.; however, it is possible that the overtones may be sensed at times instead of the fundamental, in which case the tonal quality will correspond to the overtones. When vibratory tinnitus is like a musical tone, it should be possible to obtain beats by superimposing tones of close but not identical frequency. Transitory vibratory tinnitus often automatically takes on a fluctu-

ating quality like the beating of two interfering tones. This may appear to occur in one ear or in two ears. It is sometimes heard as a tone near middle C (256 d.v.).

The type of deafness associated with vibratory tinnitus is usually conduction deafness — but the "busy wire" effect from the tinnitus as from extraneous sounds will diminish A.C. and B.C. and, therefore, simulate a nerve deafness at the frequencies of the tinnitus.

Vibratory tinnitus cannot be denied by becoming accustomed to it, accepting it as an annoyance to be borne, or by psychological treatment. It is a real sound heard by the patient, and as long as it is heard it remains a real sound and is heard in its true loudness.

NONVIBRATORY TINNITUS.

There is another type of tinnitus which is quite a different phenomenon from vibratory tinnitus. It is not an actual sound, not a real vibration. I call this type nonvibratory tinnitus. This type of tinnitus has no existence outside of the sufferer, and no existence within him except as a sensation resembling sound. It originates by local or reflex biochemical irritation, not mechanical vibrations, of the neural elements of the auditory apparatus.

Nonvibratory tinnitus is an illusion of sound. Sometimes it may be a delusion, but not permanently. The irritation causing it and the resulting sensation are real but the patient is usually aware of its autogenous origin. It is not then a delusion. I am not considering here the delusional and hallucinatory types of head sounds often experienced by the mentally ill.

Nonvibratory tinnitus is brought about by the activation of the same neural elements which are activated by real sound but the pattern is different. There is no fundamental and overtone patterns as with applied frequencies, and no masking of extraneous sounds by its overtones. It has either a scatter pattern or a block-out pattern of irritation — not an ordered frequency overtone, difference and summation tone, pattern like that set up by actual vibrations; however, like actual vibratory stimulation, its intensity, whether faint or loud, is dependent upon the number of living neural elements activated, and its frequency content upon a preponderance of irritation of definite frequency areas.

Nonvibratory tinnitus is an illusion of sound but not an illusion of irritation. It is a real sensation to the patient and when severe often the cause of much suffering. It is frequently described as very loud, sometimes as deafening and unbearable and as driving the sufferer insane. He may actually have fear for his sanity. In spite of such complaints, I have found that the tinnitus frequently measured only 5 to 10 dcb. in loudness. It was not, then, actually as loud as the patient stated, if measured in comparison with applied sound. The patient's own judgment determined the measurement. Why this discrepancy between the measured and the imagined loudness? Why this illusion of great loudness? There are many reasons, but the most obvious are:

1. Individual differences in reactions to acoustic sensations. When severe tinnitus abates to some degree, the patient retains for long periods such a vivid memory of its disconcerting persistence that he is apt to describe its loudness in terms of its greatest previous intensity, and not as of the moment of the immediate inquiry. There is a vivid memory of the noise at its worst. An accurate memory of intensity, and in most people of the frequency, of sound is difficult. A few minutes or even a few seconds' interval of relief from tinnitus may render the memory of its loudness vague or greatly different from its actuality.

2. Nonvibratory tinnitus has a real effect upon the hearing, but in a different manner than vibratory tinnitus. When it abates or ceases, the hearing usually appears more improved in the case with vibratory tinnitus, and vice versa. By actual measurements the hearing may improve or diminish as much as 40 to 50 dcb. at some frequencies. Part of the improvement is brought about by the freeing of the nerve elements originating and carrying the tinnitus impulses. While busy with tinnitus they are useless for the sensing of real sound. When not busy they are free to receive, transmit or sense sound, depending upon their position and function. Part of the improvement in hearing is due to the removal of the masking effect of the tinnitus.

In many instances a large part of the improvement is due also to the removal of the mental disturbances caused by the tinnitus, and the feeling of relief and the restoration of the ability to listen to better advantage; to listen in quiet. This is the psychological side of the reaction to loudness. It is

based on the firm foundation that when the tinnitus is less the hearing is better, and vice versa. It is the loudness of the tinnitus which then thrusts itself upon the patient's mind as the most important factor in his disability. The patient reacts to tinnitus similarly to the way most people react to annoying environmental noise. It is a hindrance to listening, to hearing and to quietude. It is disturbing.

3. The greatest improvement in hearing is due to a subsidence of the irritative lesions causing the tinnitus (not the tinnitus sensation), as well as to the co-existing lesions which, though not causing tinnitus, do cause deafness. The variance between these two factors in the causation of the deafness is one of the reasons why the over-all improvement in hearing does not exactly coincide with the frequency band of the tinnitus, and why the variations (improvement or decrease) in the hearing are usually greater in nonvibratory tinnitus than in vibratory tinnitus. The latter is not originated or transmitted by abnormal elements in the inner ear or auditory neural pathways, the neural part of the hearing mechanism being normal.

4. It is apparent that tinnitus is not caused by all of the lesions causing deafness. It is caused only by the lesions which are in the stage that precedes destruction, the stage wherein they are still capable of activation by irritation. It is the still living neural elements which cause nonvibratory tinnitus. It is the degenerated or dead elements which cause true nerve deafness.

The living and the dead nerve elements intermingle in the less severe lesions. In the severe lesions there are a few or no living nerve elements. Near the margins of a discrete severe lesion there is usually less degeneration and, therefore, more life than near the center of the lesion.

5. The loudness of the tinnitus depends upon the number of nerve elements irritated, but the sensation of loudness involves factors much more complicated than this. Aside from the number of fibres irritated, the extent or spread of the area occupied by the irritation plays a part in determining the loudness of the sensation it causes. This may be compared with a somewhat similar tactile phenomenon observed when equal weights of dissimilar dimensions are placed upon the skin (the part being supported to eliminate muscle sense).

The broad based weights will give a sensation of greater speed, and a greater superficial area tactile sensation than the smaller base weights. The touch, itch or tickle value will appear greater, although the weights be identical.

It is the greater speed which determines the greater sense of irritation because more nerve fibres appear to be irritated. This is one reason why a band of frequencies (noise) is more disagreeable and gives a sensation of greater irritation than a pure tone. The frequency spread is greater for the noise.

6. Deep troughs and steep declines in the audiometric curve show two phenomena bearing on the frequency and loudness sensations of tinnitus. The frequency area corresponding to the bottom of a trough or a dip contains the more degenerated elements, as shown by the fact that the greatest deafness is here; however, the tone of the tinnitus does not usually correspond to this frequency area unless the trough is shallow, not over 25 dcb. below normal threshold. On the contrary, it corresponds to the upper portions of the sides of the trough in the frequency areas where the more normal elements and the degenerated elements meld. Which frequency side of the trough predominates in the irritation, and therefore in the consciousness as tinnitus, depends upon the severity and spacial distribution of the lesion. In the case of precipitous dips the frequency of the tinnitus corresponds to the frequency areas near the brow of the hill.

7. I have observed that tinnitus within the frequency areas of dips and troughs is more diffused in tonal quality, and generally more annoying, the broader and less precipitous the slope of the hearing curve in the frequency areas of the tinnitus. This appears to be brought about because such hearing losses and the tinnitus are caused by lesions of the basilar membrane and because the less precipitous the curves the less concentrated or localized is the mass degeneration, and the broader the spread of irritated elements. There are, then, more elements capable of irritation in the areas of the lesions causing the deafness. These observations are based upon measurements made of the more permanent forms of deafness, and of the tinnitus due to the accompanying biochemical irritations.

8. The ear is not the only sense organ which originates and transmits illusions of sensation. The eye can originate sen-

sations of light without the presence of any light. The tongue and nose can originate sensations of taste and smell without the presence of the substance associated with taste or odor. The skin can originate sensations of touch, itching, tingling or tickling without the presence of external stimuli.

One usually refers cutaneous itching, burning or pressure sensations to the periphery of an irritated or injured area of integument. For touch sensations this is due to the nature of the stimulus; *i.e.*, a deformation and mechanical stretching of the tissue and its contained end-organs. In the case of itching, the persistent neural discharge arises from the zones of slight or moderate damage, and not from the more severely damaged or degenerated tissues. If the lesion is small, all sensation is concentrated, but with lesions of large area the spread is a prime factor in the sense of irritation. The larger the spread of the lesion the greater the annoyance from the itching, tickling or burning sensation, irrespective of the viability of the tissues in the central portion of the lesion.

Peripheral nonvibratory tinnitus may, therefore, be likened to an irritation (tingling, tickling or itching) of the basilar membrane, and its tonal quality to an irritation in particular tonal areas of the membrane.

Central tinnitus, on the other hand, may be said to represent a less differentiated or mass irritation of neural elements. The tinnitus in such mass irritations shows little resemblance to patterns obtained from the reception of actual sound, except those from mass stimulations like thermal noise. The sensations are due to the rhythmic and more or less synchronized firings of neural elements irritated by pressure, destruction or other biochemical irritations in the same way that other nerves of sensation may be activated under comparable circumstances.

The type of deafness associated with nonvibratory tinnitus is always nerve deafness, no matter what other types may be superimposed. The location of origin of nonvibratory tinnitus may usually be determined by its tonal and masking characteristics in relation to the threshold and recruitment of loudness measurements.

Nonvibratory tinnitus is associated with many disorders. It is a part of the so-called Mènière's syndrome. Acoustic

shock or other trauma to the inner ear, intracranial arteriosclerotic lesions, aneurysms, brain tumors, pressure, anoxia, changes in pH, allergic and water balance disturbances, toxic, degenerative or regenerative biochemical irritations of the auditory nerves may all cause nonvibratory tinnitus. Such irritations may act directly or indirectly, through the endocrine and autonomic nervous systems. Well known drugs and poisons causing tinnitus are quinine, the salicylates, nicotine, arsenic, phosphorus, lead, carbon monoxide and disulphide, mercury, morphine and some aniline dyes. Dosage and idiosyncrasy determine the irritation response necessary to produce the threshold or louder auditory sensation; *i.e.*, the tinnitus. Tinnitus is one of the symptoms accompanying many diseases; on the other hand, severe illness with high fever, fatal blood diseases, syphilis and brain tumors may run their courses without tinnitus.

Auditory fatigue from tinnitus or the lesions causing tinnitus may be important but little is known about it. Deafness produced from chemical irritations (poisons) is basically different from that caused by fatigue from ordinary sound vibrations. Tinnitus seldom attains anywhere near the intensities which we use experimentally to produce degeneration of the hair cells. It is usually faint, but in any event does not cause acoustic shock because it is not of vibratory origin; however, constant biochemical activation of any nerve causes some fatigue with time and constancy. It is thinkable that even when so slight that the biochemical irritations produce no audible tinnitus, they may, nevertheless, produce some fatigue. Ordinarily this factor is slow acting. I have observed several patients with almost constant tinnitus (of from five to 20 years' duration) who show a slow progressive loss in the hearing at the tinnitus frequencies but little or no change at the other frequencies.

Fatigue of the nerve elements contributes little if anything to the actual loudness of tinnitus. Theoretically it may gradually diminish it because of the exhaustion of nerve response; however, it is not the mere presence of continued activation which causes ultimate degeneration but rather the mechanical or chemical trauma from the lesions causing the stimulation. Degeneration, of course, increases the deafness and, incidentally, up to a certain stage may increase the tinnitus. In other words, the lesions causing the tinnitus are little if any accentuated by the nerve impulses they may set up;

i.e., the tinnitus nerve impulses, because there is no mechanical and little or no chemical trauma involved in the transmission of these impulses; however, the presence of tinnitus is important from a prognostic standpoint because, irrespective of its loudness, it denotes impending degeneration.

Psychosomatic fatigue from tinnitus does not really affect the hearing but it does accentuate the annoyance from the tinnitus and make it more difficult to concentrate and to pay attention to what is being said. It may greatly accentuate "the illusion of loudness."

MANAGEMENT AND TREATMENT.

To diagnose head noises as "tinnitus aurium" and let it go at that, without a careful examination to determine its etiology, contributing factors and prognosis, and without an earnest effort to discover the lesions common to it and the accompanying deafness, is unscientific and careless practice. It is, therefore, important in the treatment of the "illusion of loudness" of tinnitus to consider the treatment of the lesions causing the deafness and the tinnitus, the tinnitus as a symptom, as well as the factors involved in the "illusion of loudness"; however, we are concerned here mainly with the illusion and so the other matters will be discussed only incidentally.

Vibratory tinnitus is often temporarily influenced by measures which retard its transmission or shut off the avenue of conduction. Such measures are rarefaction or compression of the air in external auditory meatus and middle ear by the pneumatic speculum, or by Toynbee's or Valsalva's experiments, closure of the external auditory meatus, pressure upon the muscles in spasm, holding the breath, a tight band about the neck, pressure over one or both jugular veins, or the arteries in the neck, the recumbent position, moving the head forward, backward or from side to side.

It depends upon the character and place of origin of the tinnitus whether these measures increase, diminish or fail to influence it. Some of these measures may also influence non-vibratory tinnitus.

Medicines which improve the general health, and stimulating and sedative drugs may aid in relieving tinnitus, even though they do not remove the lesions causing it; the old reli-

ables were the iodides, chloral hydrate, the opiates, iron, arsenic, mercury, digitalis, the nitrates, ergot, phenobarbital, prostigmine, histamine and, of course, the vitamins are newer well known examples. All drugs which relieve the disturbances of origin in the vascular, digestive or respiratory tracts or in the muscles or joints will, of course, tend to diminish or remove the tinnitus. Such simple measures as soda bicarbonate and even hot water before meals may be most useful. Temporomandibular disorders from malocclusion, and abscessed or impacted teeth frequently contribute to tinnitus and its "illusion of loudness." Impacted cerumen and blockage of the Eustachian tube are potent factors in the accentuation of irritations causing tinnitus. The coincidental immobilization of the stapes and its oval window membrane and the pneumatic fixation of the round window membrane appear to be involved in these conditions, and treatment by removal of the impacted cerumen and unblocking of the tubes is, of course, urgently indicated.

If drugs such as arsphenamine, quinine, the salicylates, nicotine, alcohol, or caffeine are the determining cause of the tinnitus, their discontinuance will often not only benefit the tinnitus but also the deafness associated with the drug poisoning and idiosyncrasies. Smoking is today one of the chief causes of tinnitus. The relief of disorders coincidental with or related to the tinnitus directly or indirectly through the autonomic nervous system will be of help. In this connection arteriosclerosis, allergy, eczema, hypo- and hypertension may be mentioned.

It is often impossible to remove the tinnitus but, even so, its loudness may be made to appear less apparent to the patient. Carefully measure the tinnitus so that you may help the patient to realize its real loudness, and to rationalize his symptoms. Determine the masking effect on the tinnitus of applied frequencies and thermal noise so that the examiner may better visualize the location and extent of the lesions causing the tinnitus and the deafness. Teach the patient to understand the nature of his disorder so that, by the aid of proper physical, social and habit readjustments, he may overcome the "illusion of excessive loudness," and, when indicated, subject himself to proper treatment.

Drugs alone will accomplish little. All the so-called cures for tinnitus, the dubious as well as many of the medicinally

useful drugs, may succeed only because of the personal interest and success of the otologist in obtaining the co-operation of his patient. Call this a psychological effect or what you will, it is a real service to many of these patients. It is the only legitimate service in many instances.

In deafness, as in many illnesses, fear, anxiety, shame and family maladjustments may increase the real handicap manyfold. Whenever tinnitus is experienced, there is always some effect on the hearing, some deafness. It is, therefore, the duty of the physician, by imagination, courage and companionship, to rehabilitate his patient to his rightful place in society. As aids to this end, lip-reading and hearing devices are valuable. By persistent effort and co-operation, the "illusion of loudness" will diminish or disappear, the tinnitus will assume its true intensity in the consciousness and then be borne with equanimity. The relief from the illusion of great intensity will coincidentally improve both health and the ability to listen. In this way there is a gain in hearing. The patient will in truth resume a "more abundant life." Many of the so-called "cures" for deafness and some of the operations for the "restoration" of hearing appear to improve the hearing because of incidental relief from the "illusion of loudness" or because of a cessation of the tinnitus.

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A CASE OF LIPOIDOSIS CUTIS ET MUCOSAE— SO-CALLED "LIPOID PROTEINOSIS," URBACH-WIETHE.*

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The following case is reported for two reasons: *1.* because lipoidosis cutis et mucosae (lipoid proteinosis) is exceedingly rare and has only recently been described as an entity; and *2.* because several features in the present patient have not been observed or reported in the previously published cases.

As far as I have been able to ascertain, the condition now designated "lipoid proteinosis" was first recognized and accurately described as a distinct entity by Urbach and Wiethe in 1929. The disease is essentially a disturbance of the local (tissue) lipoid metabolism, often associated either with fully developed diabetes or with systemic disturbances of lipoid metabolism. Familial occurrence is common and there is frequently consanguinity of the parents of the affected children. According to Urbach, who is to be credited with the fundamental studies in this disease, the pathognomonic feature is the deposit of a particular type of lipoid. Urbach and other authors state that histochemical tinctorial reactions and reactions of relative solubility show that this particular lipoid is not ordinary cholesterol but a phosphatid, and that this phosphatid is not free but is found in chemical combination with protein. As far as I can find, from 1908 to the present, 28 cases have been reported which can, in my opinion, now be classified as conforming to the clinical and histological picture of lipoidosis cutis et mucosae (References 1 to 27, inclusive). The present case would then represent the twenty-ninth published observation.

CASE REPORT.

The patient, G. L. M., U. S. Navy, was first seen by the author at the U. S. Naval Hospital, Brooklyn, on March 11, 1941. He was 30 years old and apparently in excellent general health.

*Read at the New York meeting of the New York Academy of Medicine, Section on Otolaryngology, Jan. 21, 1942.

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, Feb. 15, 1942.

Family History: The patient's father died of tuberculosis, his mother is alive and well. There was no known consanguinity of parents or grandparents. He has two sisters, both well. There were no allergic diseases, no diabetes mellitus or diabetes insipidus, no skin diseases, no hoarseness, no known nevoid diseases, no other discoverable case of lipoidosis cutis et mucosae in the patient's family.

Personal History: There was nothing worthy of note or relevant to the present condition until 1932. During that year the patient first observed "a slight granulation of the eyelids." This was not particularly severe or annoying and did not impel him to seek medical advice. G. L. M. states that he was not hoarse as a child, and that after puberty his voice was perhaps "heavy" but by no means pathologically hoarse. The pronounced and clear-cut manifestations of the present disease were first noted on Sept. 25, 1940. Prior to this, he had been on active duty and had been treated for about 10 days by his squadron physician for a "heavy cold and severe sore throat." The acute, febrile upper respiratory infection cleared up, and the soreness of the throat disappeared. However, the patient's voice did not return to normal. There was persistent hoarseness which at times approached total aphonia. "Whitish lesions were then noted on the buccal mucosa. Tuberculosis of the larynx was among the diagnoses considered at this time and the patient was sent to the U. S. Naval Hospital at Portsmouth, Va., for study and treatment. At Portsmouth the hoarseness persisted and more lesions of

Fig. 1. Showing typical translucent nodules at edges of lids.

the mucous membranes were noted. All investigations failed to disclose an etiologic factor, and all therapeutic attempts proved unsuccessful. Because of these negative results and because neoplastic disease of the larynx was regarded as a possibility, the patient was referred to the U. S. Naval Hospital, Brooklyn, for further study. Here, studies were continued with the assistance and collaboration of Dr. Hayes Martin and the staff and facilities of the Memorial Hospital. Among the diagnoses considered at various times were rhinoscleroma, moniliasis, tuberculosis, syphilis, neoplasm and injury to the recurrent laryngeal nerve. Among the studies executed were: histologic examinations of several mucous membrane and skin lesions; and bacteriologic and mycologic studies, including in-vitro cultures and animal inoculations for bacillus tuberculosis, for rhinoscleroma bacillus and for monilias and other fungi. The many therapeutic attempts included local Roentgen rays, ultraviolet rays, medical diathermy, antisyphilitic treatment with marpharsen and bismuth, and many topical measures, including tincture of gentian violet iodine and mercurials. All attempts at treatment were fruitless.

Clinical and Laboratory Findings: On March 11, 1941, a presumptive diagnosis of lipoid proteinosis could be made on inspection and on the basis of history and clinical appearance.

The following changes in the skin and mucous membranes were recorded at this time: "the edges of the eyelids are the sites of pinhead-sized and somewhat larger, slightly translucent papules. The color of these papules ranges from that of normal skin to a more brownish-yellow. The lesions are arranged along the free edges of the lids, in pearl chain or moniliform distribution, and these changes are more marked on the upper lids and at the medial borders and angles of the eyes (see Fig. 1). The lids are thickened and the lower lip in particular protrudes. Both the vermilion border and the buccal aspect of the lips are uneven

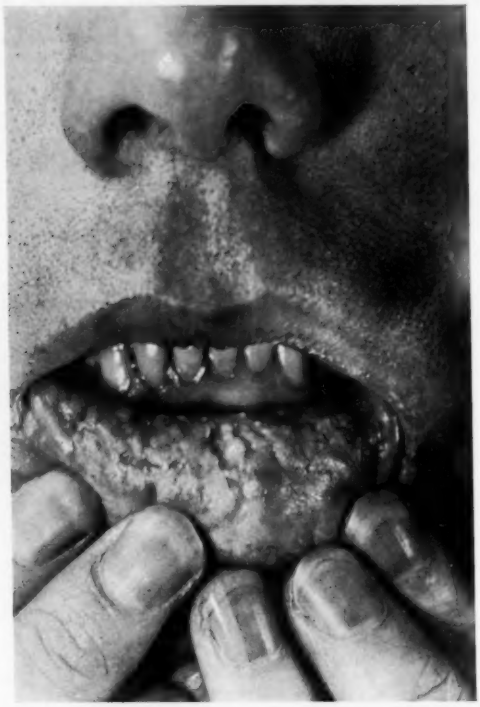

Fig. 2. Note thickening, fissuring, rugae and translucent papules on lower lip. (Courtesy of Dr. Hayes Martin, Memorial Hospital, New York.)

and deeply corrugated and present whitish-yellow papules. These lesions are similar to those on the lids but many of the individual papules are somewhat larger than those around the eyes (see Fig. 2). The mucous membranes of the inner, buccal aspects of both cheeks presents a similar rugose appearance, with thickening and papules imparting a whitish, glistening cobblestone-like appearance to the surfaces. These changes are more pronounced on the left cheek, and the orifice of Stenson's duct on the left is elevated and reddened. The tongue is much thickened and feels hard-elastic and somewhat sclerotic to the palpating finger. The surface of the tongue is rather pale and glistening and presents cobblestone-like papules and deep furrows (see Fig. 3). Complete pro-

trusion of the tongue is impossible and motility is limited both by the general thickening and by the scar-like retraction of the frenulum. The under-surface of the tongue and the alveolar folds and ridges present a thickened, glistening, uneven and cobblestone-like appearance."

According to Lieut.-Comdr. J. F. Neuberger, who was kind enough to perform the otolaryngological examination, the findings were as follows:

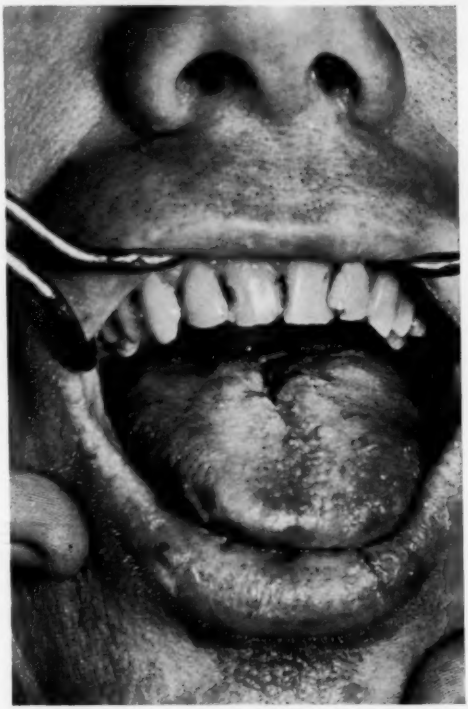

Fig. 3. Note thickening of tongue and similarity of the hemispherical translucent papules on tongue and chin. (Courtesy of Dr. Hayes Martin, Memorial Hospital, New York.)

"In the nasopharynx there is present a confluent mass of circumscribed flat papules, recognized by a lighter color of the mucous membrane covering this area. The oral pharynx does not show any of these pathognomonic papular lesions but is irregularly granular and more suggestive of a chronic process dependent on a postnasal drip.

"The epiglottis is normal. There is no thickening or limitation of motion observed.

"The mucous membrane of the right arytenoid cartilage presents a characteristic nodule on its mesial aspect, where it meets the left arytenoid on adduction. There is no marked swelling or limitation of motion. The mucosa of the left arytenoid cartilage is swollen, slightly reddened

and there is a slight limitation of motion on phonation. Both vocal cords are thickened and leathery in appearance. No ulcerations are observed and no masses seen. There is no apparent limitation of motion. The right false cord is hypertrophied and is seen partially extending over the true cord on phonation.

"No other lesions were observed."

In addition to the eyelids and mucous membrane changes, several areas of skin are affected by the process. Thus the chin, just below the lip and in the midline, is covered by ridges of minute whitish-yellow papules (see Fig. 4). The skin of both elbows and the ulnar skin strip adjacent to the elbows is lichenfied and slightly scaly and presents

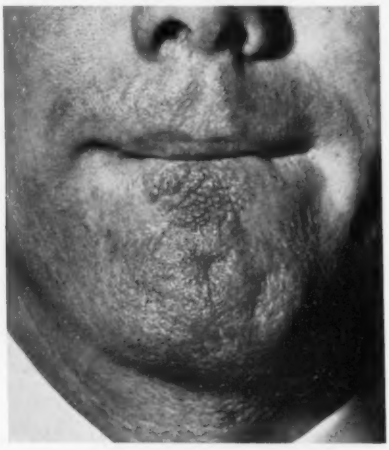

Fig. 4. Showing grouped irregular translucent papules between lower lip and chin.

cobblestone-like agminated papules of slightly yellowish-brown color. These papules are here larger and flatter than in any other affected site and impart an appearance of a moderate degree of giant lichenification (see Fig. 5). The parotid gland on the left is enlarged, the outlines clearly visible, from the external aspect. The gland is palpable and of hard-elastic consistency. The patient is extremely hoarse and can raise his voice only with some difficulty.

Complete physical examination, Roentgenologic and electrocardiographic studies all elicited normal findings. Studies for amyloidosis, either local or general, gave negative results; congo red retention was within normal limits, and there was no staining of the skin or mucous membrane lesions on local or intravenous injection of the dye. All other investigations produced normal results with the exception of the following studies of blood lipoids, as reported by Dr. Herman Sharlit on June 6, 1941:

"Total lipids	840	mg. %
Fatty acids	570	mg. %
Lipid phosphatids	6.8	mg. %
Total cholesterol	265	mg. %
Cholesterol esters	115	mg. %
Dispersion test started on pure serum extract	Reading 32	
On addition of cholesterol to extract	Reading 24	

"Interpretation: Fractional analysis reveals an important variation from normal in that the cholesterol esters represent only 43 per cent of the total as against the expected 60 or 70 per cent. This definitely represents a lipid status of the blood of lowered stability. The findings by my method, to the best of my present suspicion as to their meaning, carry this same implication."

Blood and urine contained normal amounts of all other chemical constituents. Tests for sugar tolerance produced normal curves.

A new series of biopsies were performed on lesions from the chin, from one of the elbows and from the buccal mucous membrane. The

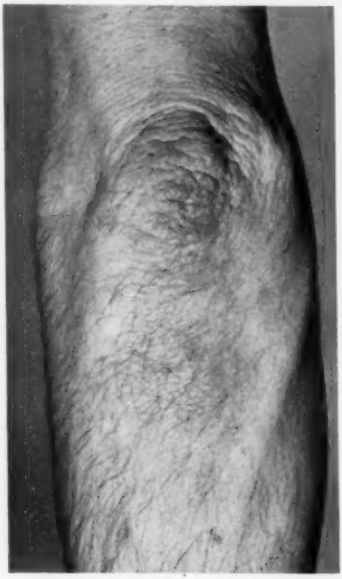

Fig. 5. Showing thickening and furrowed appearance and papules on elbow and ulnar strip.

findings in all three sites were essentially the same (excepting, of course, the expected normal absence of horny layer in the mucous membranes). Dr. Wilbert Sachs, of the New York Skin and Cancer Unit of the New York Post-Graduate Medical School and Hospital, made the following report on a hematoxylin-eosin preparation on June 6, 1941:

"In the upper cutis and the papillary bodies the vessels were dilated. For the greater part the collagen is very loose and lacy and takes a basophilic stain. The rest of the collagen takes a rather brilliant acid stain and through this area there are numerous basophilic strands, not unlike those seen in granular degeneration. There is a distinct but sparse wandering-connective-tissue-cell infiltrate. The overlying epidermis is extremely acanthotic with elongated rete pegs and with palisade layer intact. There are no other noteworthy changes."

More detailed histologic studies were carried out in conjunction with Dr. Charles Sims, of the New York Skin and Cancer Unit of the Post-Graduate Hospital. There were dilated blood vessels to be seen in the upper and middle cutis and many of these vessels evidenced endothelial proliferation. In the hematoxylin-eosin preparation these homogeneous, poorly stained areas were seen "manteling" the blood vessels and scattered throughout the cutis.

Stains with Sudan III showed that in these regions the deposits manteling the blood vessels and in the perivascular and other tissues were of lipoid nature (see Figs. 6, 7 and 8).

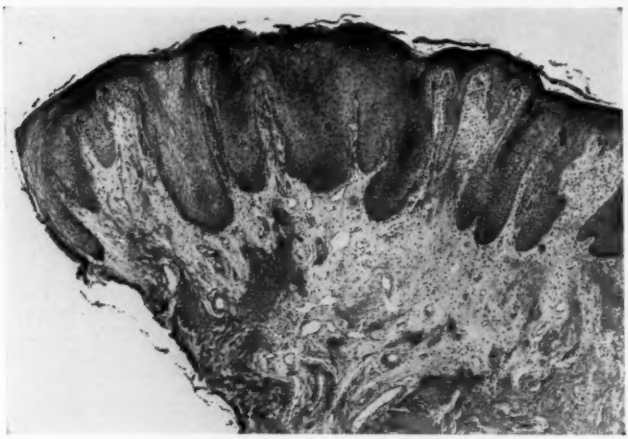

Fig. 6. Showing acanthosis, some absence of granular layer. The cutis shows areas of rarefaction and lack of staining, and these areas give positive staining reactions for lipoid. Moderate dilatation of blood vessels and sparse cellular infiltration. (Hematoxylin-eosin stain) 80x.

Dr. Max Lederer, Director of Laboratories of the Brooklyn Jewish Hospital, was kind enough to carry out special lipoid studies with histochemical methods and reports the following:

"A small fragment of skin was fixed in Bouin's solution and stained by the hematoxylin-eosin method. The epidermis shows a slight hyperkeratosis and a moderate acanthosis. The corium is composed of a dense homogeneous, amorphous, collagenous material, which is highly acidophilic, both the papillary bodies and the subcuticular connective tissue being involved. Scattered throughout are varying sized, circular and oval, clear, empty spaces lined by flat cells with prominent oval nuclei, and some thick-walled blood vessels. The former are either blood or lymph capillaries. In the altered corium are seen varying numbers of oval, vesicular nuclei but no definite cell outlines can be distinguished. In some of the vessels the adjacent tissue takes on a loose texture and deeply-pink-staining collagen fibres form a surrounding meshwork. Although for the most part the amorphous material is arranged diffusely, in some instances it occurs as narrow bands. The walls of the larger arterioles contain a similar acidophilic substance with only a few oval nuclei, no cellular outlines being visible. In some instances the walls of the vessels merge imperceptibly with the adjacent homogeneous

matrix. No cellular infiltration is seen except at the base of one rete peg, where there is a very small accumulation of round cells. No foam cells or evidences of inflammation are seen anywhere. A small area of necrosis is found in the lower edge of the specimen.

"Another small fragment was fixed in formalin, sectioned frozen and stained with Scarlet R. Here, the corium is peppered with fine, red-staining granules which are scattered diffusely in the areas corresponding to the homogeneous amorphous material seen in the hematoxylin-eosin section. The granules differ much in size, none appearing as droplets. In the papillae they are arranged in streaks which are parallel and lie in the long axis of the papillary body. The staining varies according to the density of the granular accumulations. The blood vessels are clearly outlined by bright red-staining granules which are indiscrimi-

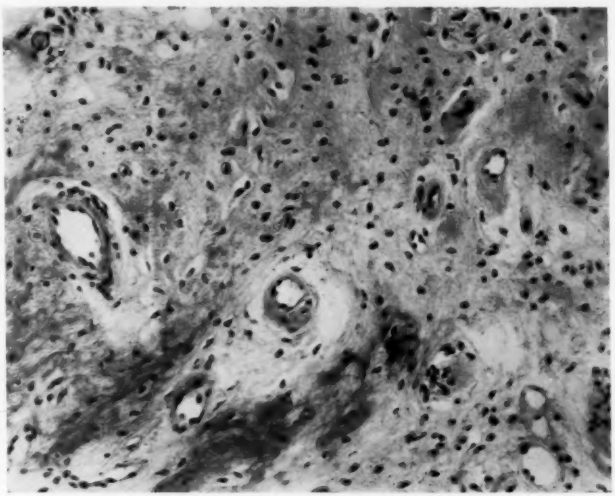

Fig. 7. Section of cutis showing rarefied areas of lipoid deposits and dilatation and "manteling" of blood vessels. (Hematoxylin-eosin stain) 375x

nately and profusely scattered throughout the walls. These granules are much larger and coarser than those seen in the connective tissue. The granules are probably some form of lipoid which is present in the collagen, and more abundantly in the walls of the blood vessels. Their exact cellular localization cannot be determined. No free fat droplets or histiocytes containing red-staining granules can be found.

"A third fragment was fixed in formalin, embedded in gelatin and stained by the Hoerr-Romeis stain. Here the amorphous material appears as a diffuse deep yellow substance. The blood vessels, however, are clearly visible by virtue of the amber hue of their walls. The latter are markedly thickened, swollen, and the material which responds specifically to the stain is amorphous, homogeneous and apparently acellular. According to the usual behavior of chemicals to this stain, the amber-colored material is said to be significant of free cholesterol.

"Because of the scant amount of materials, further studies could not be made, but the picture it presents corresponds very intimately to the

lesion found in lipoid proteinosis. The positive Hoerr-Romeis reaction for cholesterol is extremely interesting in this respect, especially since as much as 0.3 mg. of cholesterol per 100 gm. of tissue has been described by Montgomery and Havens in this condition. Personally, I know of no other instance in which this stain has been employed with the result above described."

Studies performed by Lieut.-Comdr. S. M. Rabson at the U. S. Naval Hospital, Brooklyn, gave results coinciding with the findings of Sims as reported; it is, moreover, important to note that special stains for amyloid failed to produce characteristic reactions in the infiltration.

Fig. 8. Showing lipoid deposits in upper and midcutis. Note perivascular deposits and the fine granules scattered without regular arrangement. (Stained with Sudan III.)

The sum of these histologic studies demonstrated the presence of a local lipoid disturbance in the superficial and midcutis and surrounding the blood vessels. There was no formation of giant cells, foam cells or xanthoma cells. These findings, together with the clinical picture, serve to confirm the diagnosis of lipoidosis cutis et mucosae or so-called "lipoid proteinosis," of Urbach and Wiethe.

COURSE.

During the period of my observation, from March 11 to the present time, the clinical findings remained essentially

unaltered. Early in the course of my observations there were numerous very severe acute bouts of enlargement of the left parotid. Particularly after eating, the gland would occasionally "balloon out" to tremendous proportions, so that the skin would be glistening and tense and appear to be on the point of bursting. The pain was sometimes excruciating and necessitated the administration of morphine and other opiates. The patient learned to control these swellings somewhat by means of massage on the gland area with considerable pressure, several times during the meal and immediately after eating. It is apparent that the swellings are due to a valve-like occlusion of the parotid duct, probably by the masses of "lipoid protein" in this area of the mucous membrane. The findings on Roentgenogram and on catheterization of the duct confirmed this theory. No calculus was present. Atropin proved of no value in controlling the swellings and a series of Roentgen-ray treatments was suggested in order to reduce the secretory activity of the gland. These treatments to the area of the parotid gland were carried out by Comdr. Edmisten, of the U. S. Naval Hospital, Brooklyn. A total of 950 r. filtered through 1 mm. or 2 mm. aluminum was given in fractional doses over a period of approximately two months. The result up to the present has been promising and the patient has had some relief from the very painful and disfiguring enlargements of the parotid. There were no other noteworthy events in the course of the condition. The hoarseness persisted, with occasional improvements and exacerbations. In October, 1941, over one year after he was first admitted to the sick list, G. L. M. was relieved from active duty in the U. S. Navy because of the incurable and incapacitating nature of his condition.

SUMMARY AND CONCLUSIONS.

A case of lipoid proteinosis is reported in detail. This is probably the twenty-ninth case of this rare lipoid dystrophy. The appearance and distribution of the lesions, as well as the histologic findings of lipoid in the upper cutis and about the blood vessels, were characteristic of the disease. The unusual features of this particular case included the following:

1. The apparent absence of familial occurrence.

2. The absence of pits or scars or mask-like appearance of the face.

3. The late onset (the first characteristic lesions apparently occurred on the eyelids at about the age of puberty — there was no evidence of hoarseness as a child).

4. The absence of diabetes mellitus or diabetes insipidus. (As in some of the previously described cases, there may have been partial or abortive diabetes or a disturbed general lipoid metabolism, as evidenced by the abnormol partition of blood lipoids.)

5. The marked "lighting up," extension or exacerbation of the process at the time of an acute upper respiratory infection at the age of 29 years. (Such a flare-up and extension after "grippe" or "flu" has been observed in one previously reported case.)

6. The recurrent painful swellings of the left parotid, apparently due to valve-like, intermittent occlusion of Stenson's duct.

7. The apparent presence of free cholesterol in the lesions, which, according to Lederer, is suggested by the reaction to the Hoerr-Romeis stain.

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DISCUSSION.

DR. JULIUS F. NEUBERGER (by invitation): In examining this patient, two outstanding observations were made: (1) the hoarseness; and (2) I had great difficulty in looking down his throat because his tongue was just like leather, so that I had great difficulty in pulling it out far enough to get a good look. We see quite a number of cases of black-tongue in the service, particularly in those coming from the tropics, but very seldom this leathery tongue.

We hesitated to perform a biopsy until we ascertained what the condition was, but we could not make a diagnosis of cancer without it. We sent him to

the dermatologic department, of which Dr. Sulzberger is head, and he diagnosed the condition.

A few days after I saw the patient he returned from liberty with a swelling of the cheek, which, as always, was on the left side. There was a large mass with no drainage. He had apparently learned how to manage the condition from previous attacks, for he said, "I can open it up myself." He started massaging his face, secretion began to come out of Stenson's duct, and he continued that at intervals all day for two or three days until the swelling went down to normal. He told us that he had not had the hoarseness before being called to active duty. He said, however, that it would pass away and then come back again.

We gave him constitutional treatment, and one thing that he claimed helped him, although I could see no improvement myself, was liver extract. He also said that if he was a little indiscreet and drank an extra amount of liquor, the condition became very much exaggerated and the hoarseness was much worse than before, so he had learned to regulate his actions accordingly.

DR. PAGE NORTHINGTON: I saw this very interesting patient when he appeared before the Navy Retiring Board, and it was an extremely unusual condition. I had never heard of the diagnosis before, although it is in the textbooks. In the history recited in this case, the symptoms are said to have fluctuated, but what impressed me as the general picture on the one occasion I saw him was that there was a noninflammatory type of infiltration of the lips, tongue, sublingual region, pharynx and larynx, with the appearance very much of a person with an infection of the floor of the mouth or tongue. He could not protrude the tongue, but he had no fever and did not have the appearance of being ill or in pain. He had a few fissures in the angles of the lips. It was very difficult to look into the larynx but it seemed to me that the movements of the left side were considerably restricted.

Hoarseness was the earliest symptom in this patient, as well as in the textbook descriptions. His history recorded when he came into the service stated that hoarseness was present, and he was described as having an acute upper respiratory infection, but it appears likely that the hoarseness was caused by the disease which has only recently been diagnosed. It is a very interesting problem altogether, and an extremely interesting case. We have all seen from time to time these mouth lesions which have defied diagnostic methods of considerable degree, and we are very thankful that Dr. Sulzberger made the diagnosis for us in this instance.

962 Park Avenue.

PRELIMINARY STUDY OF EFFECT OF PROSTIGMIN ON TINNITUS.*

DR. HENRY D. TATERKA, New York.

Hearing disorders have long been among the most baffling problems which confront either the general practitioner or the eye, ear, nose and throat specialist, to say nothing of the manner in which they handicap the sufferer. Much interest has been stimulated recently by the appearance of several papers citing the use of prostigmin in the treatment of deafness, tinnitus, vertigo and other symptoms related to malfunction of the auditory mechanism. Davis and Rommel,[1] in their first paper, treated 2 patients with tinnitus and 33 who complained of chronic deafness. Surprisingly good results were obtained, if one can judge from data which were almost entirely subjective and which were collected over a fairly short period of time. In a second paper[2] they made another report on 24 of the original 33 cases of chronic deafness. Out of these 24 cases, they found that seven had obtained good recovery; satisfactory improvement had taken place in six, and slight improvement in nine; whereas two developed reactions following the treatment, and medication was therefore promptly discontinued.

Hauser,[3] et al., made a study of 56 deaf patients treated with prostigmin. They admittedly chose only chronic cases (history of deafness one year or more) and in spite of Davis and Rommel's[1] statement that "improvement was brought about by persevering when hope seemed to have fled," discontinued treatment at the end of two or, in some cases, three months. Their data are extremely difficult to evaluate inasmuch as they did not correlate results with duration of treatment. Furthermore, it seems that treatment was not individualized as to dosage or duration.

Goff[4] suggested that the various dysfunctions which play a rôle in the development of tinnitus be treated. His general schedule consisted of a special diet, adequate rest, warm, dry atmosphere, correction of constipation, removal or correction of improper dentures, regulation of fluids, elimination of extraneous noises, and a ban on quinine, salicylates and

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, Sept. 12, 1941.

*From service of J. W. Hetrick, Metropolitan Hospital, New York.

tobacco. In addition, he used various specific drugs in combination with each other and with the above-mentioned regimen. Inasmuch as his report gives no indication as to what combination of the various modalities were employed in any of the cases, the tabulation of results obtained is of questionable value, although it would seem that prostigmin was of help in relieving tinnitus in almost one-third of the 23 cases reported.

There has been much written but little proven concerning the action of prostigmin in general, but it would seem, from a review of the literature, that prostigmin might play a dual rôle in the treatment of hearing disorders. Because of its supposed action on the myoneural junction[5] it is conceived that it might augment the action of the tiny ear muscles via their nerve supply. On the other hand, several recent papers, particularly those by Perlow[6] and by Scupham,[7] et al., would seem to indicate a very definite vasodilating action of prostigmin. Thus, it would seem logical to assume that the value of prostigmin may lie in its ability to produce better circulation in the ear, thus improving nutrition and hence aiding in the return to normal function. Either of these actions alone or in combination is well within the range of plausibility.

Despite the fact that there may be some question as to the accuracy of subjective data in regard to hearing acuity, a patient's declaration to the effect that ear noises have been diminished is a valuable statement. This diminution in tinnitus is probably the reason for a patient believing that he hears more acutely even though audiometric readings do not substantiate his statements.

No attempt was made to determine accurately the effect of prostigmin on hearing. The subjects selected complained of tinnitus as their chief symptom and the study was limited to the effect of the drug on this symptom. Cases were selected regardless of the type of ear condition present, and among those treated were cases of nonsuppurative, healed suppurative and perceptive ear diseases. Cases where the tinnitus was thought unrelated to the ear, such as disturbances of blood pressure, were not treated. Dosage schedule in general consisted of injections of 1:2,000 prostigmin methylsulfate two times a week and three tablets of prostigmin bromide every other day; however, doses varied according to individual needs and response. Therapy would have been con-

tinued for a longer time in those cases showing no response had not circumstances beyond our control prevented further treatment.

The following chart represents a summary of diagnosis, treatment and results as obtained in a study of 21 cases treated for tinnitus:

Name	Age	C. C.	Diagnosis	Prostigmin Treatment	Results
F. B.	56	Tinnitus 3 yrs.	O.M.P.H.	16 injs. and tablets 3 wks.	Improved
A. M.	60	Tinnitus 4 yrs.	Nerve type of deafness	15 injs.	Improved
A. Mc.	42	Marked tinnitus and loss of hearing since puberty	Otosclerosis	22 injs.	Marked relief of tinnitus
F. L.		Head noises 3 mos.	O.M.P.H. rt. N.S.O.M. lt.	27 injs.	Improved
M. K.	48	Head noises, poor hearing for 20 yrs.	O.M.P.C. A.U.	20 injs. and tablets 4 wks.	Marked relief of tinnitus
M. B.	29	Head noises 1 yr. duration	N.S.O.M.	10 injs.	Marked improvement
D. C.	53	Head noises, hearing loss 10 yrs.	Combined type of deafness	20 injs. and tablets 10 wks.	Improved
N. K.	47	Noise and poor hearing rt. ear 20 yrs.	Nerve type of deafness rt.	16 injs. and tablets	Improved
M. T.	54	Noise and poor hearing for 4 mos.	N.S.O.M.	6 injs.	Complete relief
F. W.	23	Head noises, poor hearing 1 yr.	Otosclerosis	30 injs. and tablets	Improved
B. R.	47	Head noises, poor hearing 2 mos.	N.S.O.M.	16 injs. and tablets	Improved
R. C.	18	Poor hearing, tinnitus 6 mos.	Otosclerosis	14 injs. and tablets	Improved
L. K.	42	Head noises 3 yrs.	N.S.O.M.	18 injs.	Unimproved
E. G.	50	Head noises 2 yrs.	N.S.O.M.	10 injs and tablets	Unimproved
M. M.	50	Head noises 4 mos.	N.S.O.M.	12 injs. and tablets	Unimproved
M. G.	49	Head noises 3 yrs.	N.S.O.M.	14 injs. and tablets	Unimproved
E. P.		Head noises 1 yr.	N.S.O.M.	10 injs. and tablets	Unimproved
I. H.	64	Head noises 3 yrs.	N.S.O.M.	12 injs. and tablets	Unimproved
J. S.	27	Head noises, poor hearing 2 yrs.	N.S.O.M.	20 injs and tablets	Unimproved
M. L.	28	Head noises 2 yrs.	Nerve type of deafness	10 injs.	Unimproved
J. I.	32	Poor hearing and head noises 1 yr.	N.S.O.M.	8 injs.	Unimproved

N.S.O.M.—Nonsuppurative otitis media.
O.M.P.H.—Otitis media purulent healed.
O.M.P.C.—Otitis media purulent chronic.

DISCUSSION.

Some patients obtained almost complete relief, while others were only partially helped. The improvement in several of the chronic cases was spectacular. Case 3, whose diagnosis is otosclerosis of many years' standing, is a notable example. She had been treated in many clinics with no success and was finally referred for lip-reading instruction and hearing aid. However, tinnitus was so severe that the patient was depressed and talked of suicide unless she obtained relief. Under prostigmin her tinnitus was improved to such a degree that she believed her hearing to be better. Incidentally, this is the one case in the series where symptoms would recur when treatment was stopped, and relief obtained only while getting prostigmin.

Many of the patients commented voluntarily about the improvement in hearing, but no attempt was made in this series to do audiometric studies.

CONCLUSIONS.

1. Prostigmin has proven of definite value in the treatment of tinnitus as an otological symptom and merits further investigation.

2. Twelve out of 21 patients were improved (54 per cent).

3. In evaluating the effect on any particular case, treatment should be considered for at least two months and in some cases longer. It may well be that more frequent injections, *i.e.*, three times a week, and oral doses of three tablets a day will prove of more benefit in the more stubborn cases.

4. The effect on hearing, which was noted during treatment, also merits further study with accurate audiometric determinations.

5. It is interesting to note that of the three cases diagnosed as otosclerosis, all reported improvement.

6. While all patients were not helped, no other single remedy or combination of remedies has proven as satisfactory in my experience.

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302 West 87th Street.

AN INTERESTING CASE OF FRONTAL SINUSITIS.*†

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Philadelphia.

(This is a brief report of three cases of chronic frontal sinusitis treated by external operation, the use of a sulfonamide compound locally, minimum drainage and immediate closure of the wound, without intranasal drainage.)

CASE REPORT.

J. B., a white male, age 11 years, was admitted to the Graduate Hospital on Dec. 8, 1941, with the chief complaint of tenderness and swelling over the right eye. The following history was elicited:

On June 27, 1941, five days after swimming in the ocean, the boy complained of pain over his right eye. This pain disappeared, but two days later he developed severe frontal headaches which forced him to go to bed. On the following day there was no remission of the headaches and a physician was called. Although there was no nasal discharge, there was tenderness over the right frontal sinus and nasal drops were prescribed. The next day, or 10 days after the swimming episode, he developed massive edema of the right eyelid and forehead, with alleviation of the headaches. With the edema he had a slight rise in temperature and chemotherapy was instituted. Several days later the edema had increased and a fluctuating mass was felt in the right eyelid and over the right frontal sinus, which, on July 9, was incised through the right eyebrow and pus evacuated. A drain was inserted and the wound continued to drain until Aug. 14, at which time all symptoms had subsided. X-ray examinations were made on July 10, 22 and Aug. 14.

Early in September, one of us saw the boy in the office for the first time. There had been no pain or fever since July 9, nor had there been any nasal discharge at any time. The boy had been perfectly well except for the fluctuating mass in the right frontal region, and he had just started in the fall term at school. Since there were no subjective symptoms at this time, the parents did not favor any surgical procedures. However, he was kept under observation and on Nov. 29 another X-ray examination was made. On Dec. 4 he developed some tenderness and more swelling over the right frontal region and in the right eyelid, and inflammation of the scar of the drainage incision. Operation was advised and he was sent to the hospital.

Physical examination on admission revealed a well developed, although somewhat obese, boy, age 11 years. He appeared to have no pain and answered questions readily.

There was marked thickening of the soft tissues over the right frontal sinus and the right eyelid was puffy. Inflammation of the incisional scar was present. On palpation there was slight tenderness over the frontal region and definite fluctuation over an area the size of a half-dollar. Anterior rhinoscopy revealed a normal looking nose in every respect and no discharge was observed.

X-ray Evidence: The first group of X-rays, those taken on July 10, 22 and Aug. 14, showed cloudiness of both frontal sinuses together with a progressive osteolytic process involving the anterior wall of the right frontal sinus and extending into the frontal bone some 4 or 5 cm. above the upper limit of the sinus. The X-rays taken on Nov. 29 revealed the

*Read before the Philadelphia Laryngological Society, Jan. 6, 1942.

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Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, March 10, 1942.

left frontal sinus to be clear but showed clouding of the right frontal sinus. Bony sequestra were noted and the diploe and external cortex of the frontal bone for several centimetres above the sinus appeared to have been replaced by sclerotic bone as the result of the previous infection.

On Dec. 9, the day after admission, a radical frontal operation was performed. An incision was made through the right eyebrow, the periosteum elevated and the frontal bone exposed. A large cavity filled with pus and granulations was found, but it was external to the sinus. The pathological process could now be seen to extend over the midline, therefore the incision was extended through the left eyebrow. The left frontal sinus was then entered and the anterior walls of both frontal sinuses were removed, as they were definitely softened. The mucosa was thickened and inflamed but there was no pus present and the nasofrontal ducts were patent. The remaining diseased bone and the fistula in the eyebrow were thoroughly curetted and all mucous membrane removed. Two semirigid rubber drains, into which fenestra were cut, were placed in the wound, one being brought out through each end of the incision. The wound was packed with sulfathiazole powder and an obliterating closure was made. Since the nasofrontal ducts were patent, they were not disturbed.

Pathology: The anterior wall of the frontal sinuses was composed of diploic bone. An osteolytic process had destroyed the anterior surface of this bone to a point about 5 cm. above the roof of the right frontal sinus and somewhat laterally in both directions. A secondary sclerosing process had then taken place as a result of the original inflammation. The mucous membrane lining of the sinuses was thickened and showed signs of recent disease. Between the skin and periosteum and the partially necrotic bone of the right frontal region was a large abscess cavity filled with granulation tissue and pus.

The postoperative course was quite uneventful. The only local reaction was a moderate edema of the left lid, which cleared up spontaneously in several days. Chemotherapy in the form of sulfathiazole and to the extent of 0.5 gr. per pound of body weight per day was given as a precautionary measure for six days. The sutures were removed in six days and the drains in nine days. A small amount of serous discharge was present for a few days. Since the supraorbital ridges had been left intact at operation, there was very little deformity. The patient was discharged from the hospital on the eleventh day with the wound healed, and on this date, March 15, 1942, the site of operation is normal in appearance.

Conclusions: This case, we believe, is one of acute frontal sinusitis with extension of the infection into the diploe of the frontal bone. This osteolytic process was apparently localized and self-limited. After the acute infection had subsided, about six weeks after the onset of the symptoms, a sclerosing process, evidence of which is seen in the X-rays of Nov. 29, took place and was noted at the time of operation. The cortex of the anterior plate of the right frontal sinus, however, had been previously destroyed after perforation from the sinus had occurred.

Comment: Several features of this case seem to warrant a report and brief discussion.

1. The length of time that elapsed between the original infection and the operation, with no general symptoms for nearly four months. During all of this time there was a large area of fluctuation over the right brow, but at no time any nasal discharge. Probably the chemotherapy administered at

the onset of the disease had cleared up the infection in the sinuses after perforation had occurred and had also limited its spread through the diploic bone, which was finally sealed off by the sclerotic process observed in the later X-ray studies.

2. The presence of an osteomyelitis of the anterior plate, which could only have taken place if this plate was diploic, and the destruction of the outer cortex, the inner plate of the outer wall remaining intact. There were several sequestra observable in the X-ray plates representing the remnants of the cortex.

3. The method of treatment and its results. A classical external frontal sinus operation was performed on both frontal sinuses, with beveling of the bony edges, preserving most of the supraorbital ridges but removing the chronically inflamed and infected mucosa. Since there was no secretion present, the nasofrontal ducts were normal in appearance, there was and had been no nasal discharge and there was no intranasal pathology, the ducts were not disturbed. With us, in the past, it has been customary in radical frontal sinus operations to enlarge the ducts with gouge or rasp and insert rubber tube drainage into the nose. The difficulty has been to keep the ducts patulous even when the Lothrop procedure was followed. In this case the entire cavity was filled with sulfathiazole crystals and a fenestrated drainage tube passed through the cavity to exit at the lateral margins of the skin wounds above the external canthi. Except for these openings the entire skin wound was closed accurately. We were led to use this method because we had previously employed it with most satisfactory results in two cases; one in 1937, a case of cholesteatoma, and the other, early in 1941, a case of semichronic frontal sinus infection of several months' duration. Neither of these cases had any intranasal pathology and both of them healed in a remarkably short time — less than two weeks — and without deformity. One of the writers was an early advocate of the blood clot method of closing mastoid wounds and, from his experience of many years in this procedure, it seemed to him that it might apply equally well to the frontal sinus, and it was in this belief that it was first tried. The local use of the sulfonamides in other conditions strengthened this belief, and, so far as is known, these cases are the first ones so treated. The results have at the least exceeded our expectations.

1721 Pine Street.

A CASE OF SUBARACHNOID HEMORRHAGE SIMULATING ACUTE FRONTAL SINUSITIS.*

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The case to be presented illustrates how an intracranial lesion may simulate sinusitis to the extent of most detailed symptomatology. Cohen[1] reported a case of adenoma of the pituitary that had been previously diagnosed posterior sinus disease, and the patient had been subjected to intranasal surgery. In the light of our present knowledge, chemotherapy offers most to a patient suffering of subarachnoid hemorrhage with reactive meningitis. An early diagnosis leading to the administration of adequate doses of a sulfonamide would, therefore, go a long way towards the assurance of a favorable outcome. As the meninges are not equally permeable to the various sulfonamides, it is worth recording that sulfanilamide was the therapeutic agent of choice in our case. Through a careful study of our patient we were able to establish arteriosclerosis as an etiologic factor in subarachnoid hemorrhage, and we found the cholingeric components of vitamin B to be of decided benefit in the relief of headache in this type of an individual.

CASE REPORT.

A. C., white, male, age 53 years, was admitted on Sept. 17, 1941, to the Mount Sinai Hospital on the service of Dr. A. H. Persky, with the complaint of severe frontal headache, most marked late at night, the pain increasing in intensity after 2:30 A.M. The temperature on admission was 99.6°, pulse 98, respiration 22.

The trouble began one month before admission, following an emotional upset. The headache was increasing in severity as time went on and was now no longer relieved by aspirin and codeine.

Physical examination was essentially negative except for chronic bronchitis, with the possibility of bronchiectasis. The patient was well nourished and alert. Blood pressure, 135/80. Rhinoscopic examination disclosed slight redness of the mucous membrane but no free pus was seen. The nasofrontal ducts were patent, but the patient experienced relief on probing the frontal sinuses and the application of cocaine to the nasofrontal ducts. Nasopharyngoscopic examination showed some thickening of the posterior portions of the middle turbinates. The pharynx was congested. On transillumination all the sinuses appeared

*Presented at the Staff Meeting of Mount Sinai Hospital, Jan. 22, 1942.

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, March 15, 1942.

clear. X-ray disclosed cloudiness of the left maxillary and left ethmoids; however, on puncturing and washing the left antrum, no pus was obtained. The blood count, urinalysis and blood chemistry showed no gross abnormalities. The blood Wassermann and blood cultures were negative.

The diagnostic possibilities considered were frontal sinusitis and an intracranial accident. The localization of the headache and its nocturnal aggravation favored the diagnosis of an acute infection of the frontal sinus, but several elements in the clinical picture did not fit into this condition. These were the patulous nasofrontal ducts, the absence of pus, the prolongation and increasing severity of the illness and the history. Another argument against the diagnosis of acute sinusitis was the fact that the patient's low grade fever of a month's duration was not influenced by chemotherapy, an intensive course of sulfathiazole having been given for a week prior to admission. However, the lumbar puncture, which was done on the day following admission, clarified the diagnosis. The spinal fluid was xanthochromic; pressure, 220 mm. by water manometer; W.B.C., 18; sugar, 65 mgm. per 100 cc; globulin, +1; R.B.C., 1,070. The last mentioned finding could be accounted for by trauma from the puncture. The spinal fluid Wassermann was negative, and the culture was sterile. Two days later the spinal fluid showed 63 W.B.C. with polymorphonuclears predominating, while the other findings were about the same. The temperature, however, rose to 101°, while previously the febrile level was around 100°. The patient was now placed on sulfanilamide therapy and in 32 hours the temperature came down and stayed at a normal level. Sulfanilamide therapy was continued, however, for a week subsequently until Sept. 29, 1941. The blood concentration of sulfanilamide was 6.8 mgm. per 100 cc., while that of the spinal fluid was 5 mgm. per 100 cc. Additional therapy consisted of several daily injections of concentrated glucose intravenously, and sedation. On Sept. 24, 1941 — one week after admission — the spinal fluid was perfectly clear and the pressure was 200 mm.; 51 W.B.C. were found, most of which were polys. The patient, however, was now symptom-free. On Oct. 2, 1941 — 15 days after admissioun — 35 cc. of clear spinal fluid under pressure of 284 mm. by water manometer was obtained on lumbar puncture. The cell count was 20, and reducing substance was present. The specific gravity was 1.008, and the sulfanilamide concentration 0.8 mgm. per 100 cc.

The diagnosis of subarachnoid hemorrhage appeared most plausible. In our search for a predisposing cause, we did a platelet count, coagulation time, bleeding time, prothrombin concentration and the tourniquet test, but no evidence of a hemorrhagic diathesis was detected. X-ray of the skull was negative for fracture. The ophthalmologist, however, found angiosclerosis of the retina, notwithstanding the fact that the patient's blood pressure was always a low normal. We observed, furthermore, that the specific gravity of the urine had been consistently very low. Accordingly, a Fischberg test was done. The result obtained was a rather fixed specific gravity at 1.007 to 1.012. The urea clearance, however, was 100 per cent.

On Oct. 4, 1941 — 17 days after admission — the patient requested his release from the hospital. He had been symptom-free for 10 days prior to discharge. On Nov. 12, 1941, after having been absolutely symptom-free for five and one-half weeks, the patient returned to the hospital with the same complaints he had on his previous admission. The pain was localized about the right frontal sinus and right orbit. The temperature was 101°. All the studies done previously were now repeated and the results were about the same. No pus was seen in the nose and the nasofrontal ducts were patulous. The spinal fluid, however, was now under no increased pressure; it contained only 10 W.B.C., and all the other findings were normal. Sulfanilamide therapy was once more effective, the temperature coming down to normal in 48 hours; the concentration obtained was 7.5 mgm. of sulfanilamide per 100 cc. of blood.

As our repeated studies indicated arteriosclerosis to be the predominant etiologic factor, we resorted to cholinergic drugs for the treatment of the residual headache on the assumption of its being of a vascular origin. Following the procedure of Atkinson,[2] we chose the parenteral administration of nicotinic acid and thiamin chloride. By combining B_1 with nicotinic acid, a mild vasodilation effect is obtained, obviating the violent untoward reaction occasionally experienced when the latter drug is given alone. The injection consisted of 50 mgm. of thiamin chloride and 50 mgm. of nicotinic acid, and the results were striking. The headache disappeared after the second dose. The lumbar puncture done on admission constituted the only spinal drainage the patient obtained during his stay in the hospital. An uneventful and smooth recovery was brought about by sulfanilamide and the parenteral administration of nicotinic acid and B_1. The patient was discharged on Nov. 24, 1941, 12 days after admission. He was seen on Dec. 31, 1941, and was found to be enjoying good health.

Comment: The patient's symptomatology justified a diagnosis of acute frontal sinusitis, save for the fact that the nasofrontal ducts were patulous, which finding is not in keeping with protracted pain referable to sinusitis. The continued fever and the predominancy of polymorphonuclears in the spinal fluid are arguments for a low grade infection of the meninges. Wilson and Bruce,[3] however, cite a case of subarachnoid hemorrhage in which the fever fluctuated for a month, the febrile state being attributed to "resorption." Lassen and Vanggaard[4] found polymorphonuclear pleocytosis predominating in the spinal fluids of 43 cases of subarachnoid hemorrhage. However, the relapse which occurred after five and one-half weeks of apparent recovery recalls to mind the many reported cases of recurrent attacks of meningitis, with mild manifestations, occurring three to four weeks after the discontinuance of chemotherapy. In all of these cases a second course of a sulfonamide succeeded in establishing a permanent cure. The clinical course in our patient is parallel and points to his having had a localized traumatic or hemorrhagic pachymeningitis, notwithstanding the fact that we have no anatomic specimens to prove our case. Some degree of encephalopathy must also have been present as the spinal fluid was always copious and under increased pressure on most lumbar punctures.

Sulfanilamide produced dramatic results in 32 hours, whereas sulfathiazole administered for a week had no effect whatever. This observation, however, is quite in keeping with the known characteristics of the sulfonamides, that one derivative will occasionally be most successful in a given condition, while another one will fail. Spinal drainage undoubt-

edly contributed to the recovery, but three lumbar punctures had no influence on the febrile course until sulfanilamide therapy was started. One explanation for the ineffectiveness of sulfathiazole in our case is the fact that it concentrates only one-third as well in the spinal fluid as in the blood, according to Strauss[5] and his co-workers, whereas the sulfanilamide concentration in the spinal fluid is 75 per cent as compared to the blood. Moreover, sulfanilamide stays longer in the body than sulfathiazole, the latter drug being excreted rapidly in the urine. In our case the spinal fluid retained a concentration of 0.8 mgm. of sulfanilamide per 100 cc. of spinal fluid — four days after the administration of the drug was stopped. The mode of action of sulfanilamide in this case — in the absence of bacterial invasion — may be explained on the theory that sulfanilamide exerts a beneficial effect on an inflammatory process.[6]

Arteriosclerosis was undoubtedly a contributing factor in the development of subarachnoid hemorrhage in this patient as our studies showed him to have nephrosclerosis and angiosclerosis of the retina. Speedy relief from the residual headache was obtained from the parenteral administration of thiamin chloride and nicotinic acid. The cholingeric action of these drugs is responsible for this effect, which constitutes a therapeutic confirmation of the etiology.

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529 Snyder Avenue.

PROLAPSE OF THE LARYNGEAL VENTRICLE IN ACUTE MYELOGENOUS LEUKEMIA. REPORT OF A CASE.

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The subject of prolapse of the laryngeal ventricle is not even mentioned in some textbooks of laryngology.[1,2,3]. Others[4,5,6,7] just give a short description of the condition. Jackson and Jackson[8] discuss the subject briefly. Moore[9] has so far made the most comprehensive and complete review of the subject when he collected 82 cases reported in the literature up to 1929. According to him, much confusion and ambiguity exists as to the nomenclature adapted in connection with the subject. "Prolapse of the ventricle" was introduced in laryngological terminology by Lefferstein in 1879, and that of "eversion of the sacculus by Moxon in 1868. Moore defines "prolapse of the laryngeal ventricle" as the protrusion of a portion of the ventricular mucosa as a result of inflammatory edema or hyperplasia, so that parts of the ventricle normally out of sight are carried inwards along with the swelling and come to be brought into view of the laryngoscope. It is therefore used to describe a condition of varying etiology. Forkner,[10] in his book, "Leukemia and Allied Disorders," mentions Seelenfreud (1925), who collected from the literature 40 cases of both acute and chronic leukemia with leukemic infiltration of the upper respiratory tract. Although the larynx was the site of the most frequent location of the lesion, he said that the order of frequency of involvement was: *1.* epiglottis; *2.* subglottis; *3.* false vocal cords; *4.* true vocal cords; and *5.* arytenoids. He did not even mention the ventricle. It seems, after searching in the literature, that no case is yet reported of prolapse of the laryngeal ventricle in acute myelogenous leukemia. Hence this case is reported.

CASE HISTORY.

V. A., age 20 years, male Filipino laborer, was admitted into the Philippine General Hospital on Nov. 10, 1939, with bleeding from the gums and generalized body weakness for two months. A week before he entered the hospital the bleeding became more profuse especially on awakening in the

Editor's Note: This ms. received in Laryngoscope Office and accepted for publication, June 20, 1941.

morning. Two days later, he noticed purpuric patches, first in the upper extremities and then in the other parts of the body. From the onset of the illness he had intermittent low grade fever, sore throat and increasing pallor. On the day of admission he developed profuse bleeding from the gums. He had had malaria in 1937; no other diseases of importance.

On admission, he appeared fairly developed but pale. Teeth were in good condition. Gums were pale, soft, slightly tender with bleeding margins. Blood clots were present between the teeth. Pinhead, petechial hemorrhages were present in the left tonsil and posterior pharyngeal wall. The tonsils were not enlarged. Some submandibular glands in

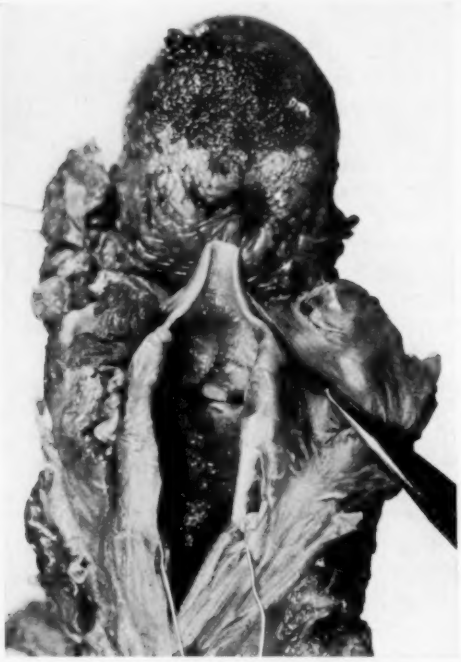

Fig. 1. Posterior wall of larynx cut open to show the prolapse.

both sides were slightly enlarged. A localized cardiac systolic murmur was heard at the left third interspace. Lungs were normal. Liver was not palpable. Spleen was enlarged, with its lower border about two fingers' breadth below the left costal arch. In the skin of the extremities, chest, back, neck and face were purpuric spots varying in size from a pinhead to a corn grain. Hemogram, myelogram and peroxidase tests showed conclusively acute myelogenous leukemia.

Three weeks after admission, Dec. 3, 1939, he began to have frequent and distressing cough which disturbed his sleep. On Dec. 26 he became hoarse, and his cough had a peculiar barking character. Three days

later, direct laryngoscopy revealed prolapse of the right ventricle. The left vocal cord was congested. The prolapse did not extend throughout the whole ventricle but involved only the anterior portion. Attempt to reduce it by a probe during direct laryngoscopoy failed because of the violent cough.

On Jan. 19, 1940, or about three weeks later, the prolapse seemed to have decreased slightly and the voice was a little better but still hoarse. On several occasions the patient had bleeding from the gums and nose. He had intermittent fever throughout his stay of about 10 weeks in the hospital. He became gradually weaker and died Jan. 23, 1940, after having received several blood transfusions.

Fig. 2. Prolapse of the ventricle reduced.

The autopsy confirmed the diagnosis of acute myelogenous leukemia with infiltration of myelocytes in the different visceral organs. The larynx was obtained and dissected. The diagnosis of prolapse of the anterior portion of the ventricle was conclusively verified. The swelling which seemed solid could be reduced partially. The sacculus laryngis was dissected and it was found to have slightly thickened mucosa. There was no doubt, therefore, that the swelling seen in life by direct and indirect laryngoscopy represented a protrusion of the anterior portion of the mucosa of the right ventricle and not of the false or true cords, the subglottic mucosa nor the sacculus laryngis. Figs. 1, 2 and 3 show the gross specimen of the larynx. Figs. 4 and 5 show the photomicro-

graph of the prolapse. The pathologist, Dr. W. deLeon, described it as follows: "There is hyperplasia of the mucosa of the prolapsed ventricle, including the epithelium and mucous glands. There is a more or less diffuse infiltration of myelogenous cells (myelocytes and myeloblasts) in the tissues, together with the leucocytes of inflammation." Histologically, therefore, the prolapse is an inflammatory hyperplasia of the mucosa with diffuse infiltration of myelocytes and myeloblasts.

COMMENT.

Oppikofer[11] decries the singular lack of histological section in most cases of prolapse of the laryngeal ventricle reported

Fig. 3. The ventricle and sacculus dissected.

in the literature. This might be due to the fact that few of these cases die and are followed to the autopsy. The histological examination of the prolapsed laryngeal ventricle of the case reported confirms the general view that the prolapse is more of the nature of an inflammatory hyperplasia of the mucosa. It contributes another factor hitherto not mentioned

in the literature, that of infiltration of the ventricle with the cells of myelogenous leukemia.

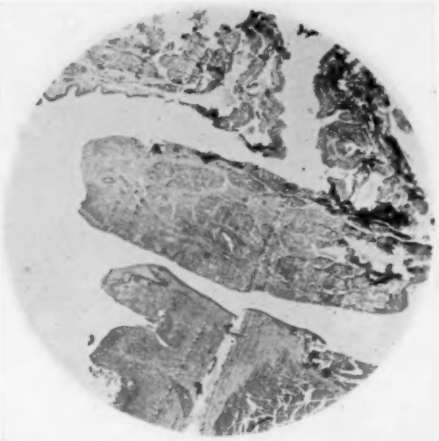

Fig. 4. Photomicrograph of prolapse; low magnification.

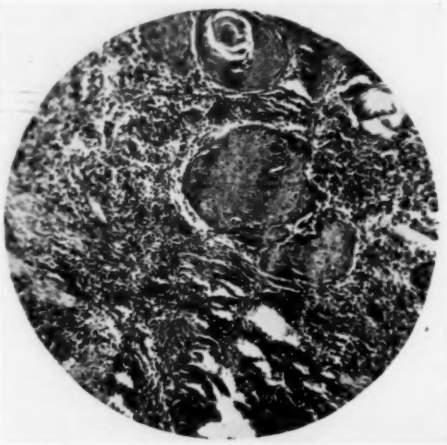

Fig. 5. Section of prolapse showing infiltration of leucocytes, myeloblasts and myelocytes.

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REVIEW OF THE 1941 LITERATURE IN THE FIELD OF BRONCHOESOPHAGOLOGY.

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Bronchology and esophagology are terms being substituted for the term peroral endoscopy in the discussion of the literature of this field of medicine. This at once lends a broader scope to these subjects, in keeping with the trend that may be observed in reviewing the literature dealing with the tracheobronchial tree and the esophagus. The advances made in thoracic surgery during the past 10 years have placed new emphasis on the importance of bronchoscopy and esophagoscopy, and consequently have placed greater responsibility on the bronchoesophagologist for early, accurate diagnosis of pulmonary and esophageal pathology and for an evaluation of functional changes upon which a therapeutic regime may depend.

Before discussing the trachea, bronchi and esophagus separately, certain topics may be presented which concern the field of bronchoesophagology as a whole. Discussions of foreign bodies in the air and food passages are prominent in the literature but a review of this nature will not permit listing the many case reports. Interest in this subject may be judged by the fact that the *Quarterly Cumulative Index Medicus* lists 61 articles published in 1941 dealing with this subject. Chevalier Jackson and Chevalier L. Jackson[1] summarize the problem of foreign bodies of the lung, dividing them into two classes: inspirated foreign bodies and penetrating foreign bodies. The two classes differ in almost every clinical feature. Penetrating foreign bodies are usually projectiles and may be removed bronchoscopically if no other indication for opening the chest exists, if the size of the bronchus tributary to the invaded lobe permits. Removal of inspirated foreign bodies has been revolutionized by bronchoscopy. All should be removed rather than allowed to remain for encystment, which is a remote possibility, or suppuration, which is a certainty. The dangers of foreign bodies remaining in the air passages are *impending asphyxia,* which is diagnosed by known symptoms and cardinal signs; *potential asphyxia* due

to failure to recognize the presence of the *symptomless interval,* after which asphyxia may develop, when, for example, an endobronchial foreign body suddenly becomes dislodged from the bronchus and impacted in the glottis. The relationship between those objects which produce an emergency and the ones which do not produce an emergency are discussed. The Jacksons emphasize that a well planned and carefully executed peroral bronchoscopic procedure will be successful in close to 100 per cent of the cases of inspirated foreign bodies.

Richards[2] points out that vegetal foreign bodies comprise a form of foreign body easily and frequently aspirated by children. Inquiry into the possibility of aspiration of a foreign body should be made in any case of unexplained pulmonary pathology, as the history, physical and X-ray findings are very typical in this condition. Bronchoscopic removal is by no means easy in most cases, the technical difficulties of removal in part being due to localized reactions to the foreign body itself or to fragmentation when grasped by forceps. The author states that postoperative reactions sometimes require tracheotomy or intubation. Forty cases of vegetal foreign bodies are reviewed in detail, peanuts being the object aspirated in 90 per cent of these cases, most of them in children under 4 years of age. The outstanding physical findings, a summary of physical signs, sojourn, the number of bronchoscopies necessary to relieve findings, the complications and the end-results of treatment are presented.

Photography of many of the body cavities has become a well recognized, routine method of recording their normal anatomy and diseased states. To photograph the tracheobronchial tree and esophagus through the bronchoscope and esophagoscope, Brubaker and Holinger[3] developed special motion picture equipment permitting constant visualization of the field, axial illumination and a relatively great depth of focus. A magazine loading 16 mm. camera is used with Kodachrome film. The light source is a ribbon filament lamp whose rays are reflected onto the main axis of the instrument. The lens is an 8 cm. focal length Zeiss tessar F:2.7 lens, operated at F:4.5. With this equipment, the landmarks of the bronchi seen in routine bronchoscopy are easily identified. The esophagus may be photographed practically to the stomach.

THE TRACHEA.

The compression of the trachea by vascular lesions is reported by Gonzales Bosch and Polak,[4] who described a case of asphyxiant compression of the trachea by an aneurysm of the horizontal portion of the aorta, and by Muratti,[5] in whose case the compression was due to an aneurysm of the innominate artery. Such case reports emphasize these lesions as contraindications to bronchoscopy. Bence[6] describes cases of tracheal varices as a different type of vascular lesion involving the trachea. Hammond[7] reported a case of a boy, age 15 years, who had had clinical and Roentgenological findings of a mediastinal tumor which was producing compression stenosis of the trachea. Intrabronchial invasion was found on bronchoscopic examination and the material removed for histologic examination established the diagnosis of Hodgkin's disease invading the trachea and right bronchus. The value of laminographic study of the trachea was beautifully illustrated by Roentgen films which demonstrated the obstruction. A case of congenital stenosis of the trachea is presented by Wolman.[8]

A practical procedure for those not accustomed to performing emergency tracheotomies is given by Hill,[9] consisting of the use of an airway such as a Mosher life saver during the operation. He advises the use of a Mosher punch or some similar instrument to assure a proper opening into the trachea.

Abbate[10] discusses the extraction of bronchial and intratracheal foreign bodies by the tracheotomy route, followed by immediate suture of the trachea. This is mentioned here only to condemn the procedure as obsolete.

THE BRONCHI.

Anatomy: Anatomical investigations of the arrangement of the bronchi has received considerable stimulus during the past year due to an increasing appreciation of the significance of the segmental divisions of the lobes of the lungs. Demonstrations of the results of these investigations were presented by means of models and specimens at meetings and will undoubtedly appear in the literature of the present year.[11,12,13] Because of the importance of these demonstrations it is felt they should be mentioned in this review.

Physiology: Significant physiologic research has had prompt acceptance in clinical application during the past year. Young and Gilbert[14] demonstrated the action of aminophylline (theophylline-ethylene-diamine) on isolated bronchial rings and on intact guinea pigs. They found that aminophylline exerts a protective action against the bronchial constrictor effect of histamine, and in guinea pigs against histamine shock and, to a lesser degree, against anaphylactic shock. The action was directly on the bronchial musculature.

Phillips, Adams and Hrdina[15] discuss the physiologic adjustment which takes place in sublethal reduction of the lung capacity in dogs. An extremely high degree of respiratory reserve was demonstrated by the fact that through a slow reduction of lung volume by resection, healthy dogs remained well and active after a reduction of volume of normal lung to 15 per cent had been accomplished. Compensatory emphysema results and is associated with other cardiorespiratory measures, such as an immediate increase in hemoglobin and red blood cell count.

Andrews[16] described a method of examining respiratory function which uses a Benedict-Roth metabolism apparatus, modified essentially by the addition of a high-speed recording drum. By this means the qualitative characteristics of respiration may be demonstrated. Respiratory obstruction in the larynx and trachea showed symmetrical slowing of inspiration and expiration at the extremes of the vital capacity tests. Bronchial asthma was characterized by a curved expiratory tracing, and obstructive emphysema by a moderately slowed velocity and trapping of air on successive maximum expiratory movements. The examination was of therapeutic usefulness, inasmuch as short periods of therapeutic trial could be made under controlled and measured conditions, thereby permitting the selection of therapeutic procedures which had been demonstrated to be effective. The effects of oxygen, helium, positive pressure, epinephrine by inhalation, and various drugs were presented. The course of an obstructive disease may be followed by this method, and the continued effectiveness of therapeutic procedures may be evaluated. The correlation between the results of the functional examination and the bronchoscopic findings was considered as of value in clarifying our knowledge of the nature

of the obstructive diseases. The effects of bronchial obstruction on the ventilation of the lungs, on the heart and on the patient as a whole were further discussed[17] and the mechanism of the four types of bronchial valvular obstruction was illustrated.

Basch, Holinger and Poncher[18] studied the physical and chemical qualities of sputum and factors determining variations in portions from different parts of the tracheobronchial tree. They found that the sputum from the most dependent parts of the bronchi had an extremely high viscosity and could be obtained only by bronchoscopic aspiration. The secretion at a higher level was the secretion from below, liquefied and with a lower solid content. On top of this secretion, after a rest period, there was found a plug with a moderately high viscosity. The various factors which influenced the character of the secretions were selective secretion, selective resorption, the speed of movement of secretion from one level to another, and bacterial action. Using these findings as controls, these authors studied the influence of the commonly used expectorant drugs, steam, carbon dioxide and oxygen in the sputum in different areas of the trachea and bronchi, and on the mucous membranes.[19] Ammonium chloride, potassium iodide, fluid extracts of senega and ipecac and emetine hydrochloride liquefied the sputum in the upper bronchi consistently but did not influence the material in the peripheral bronchi. Steam inhalations and an atmosphere of 80-90 per cent relative humidity at 70-75° F. liquefied the secretions throughout. Carbon dioxide inhalations liquefied secretions and stimulated resorption. Thus, carbon dioxide and steam may be considered as extremely efficient expectorants. Oxygen, on the other hand, unless humidified or diluted with 10 per cent carbon dioxide, thickened the secretion, as did atropine sulfate and codeine, and consequently oxygen must be considered as an antiexpectorant when administered in the treatment of respiratory obstruction complicated by pulmonary suppuration.[20]

Windle[21] has described the physiology of respiration in the fetus and believes that visible respiratory movements in the fetus, if seen, are evidence of anoxemia of the fetus and may warn of impending danger. Windle states that the physiology of respiration in the fetus is quite similar to that of the newborn and adult.

Asthma: The rôle of the bronchologist in the management of bronchial asthma is of considerable interest. Prickman and Moersch[22] have emphasized the significance of complete bronchial obstruction occurring in the course of attacks of bronchial asthma. The symptoms and signs of such obstruction are severe, persistent, sometimes paroxysmal coughing attacks which aggravate the asthma. The sputum, which at first is slight, may become profuse later and may be bloody. Fever is usually present, with or without chills. Signs of atelectasis are characterized by suppression of breath sounds and fremitus, usually occurring in the lower and posterior portions of the thorax. Roentgenological evidence of atelectasis or occasionally bronchiectasis may be present. Prickman and Moersch believe that bronchostenosis is the principal indication for bronchoscopy in bronchial asthma. The usual bronchoscopic findings are thick, tenacious mucus and the stenosis which can be dilated with forceps, thus releasing the retained secretions. Bronchostenosis may complicate asthma at any age and its incidence in their series of 60 cases was high.

Craige[23] reports in detail seven patients with bronchial asthma who died during and because of their status asthmaticus. He confirmed the five pathological characteristics of the bronchial wall previously shown to be present in asthma; namely, widened basement membrane, an infiltration of eosinophils, a widened submucosal layer, hypertrophy of muscle and a degeneration of the mucous glands. In addition, he emphasized the presence in six of the seven cases of characteristic thick, tenacious, elastic bronchial exudate. He was unable to find any relationship between the patients' deaths and the administration of atropine, morphine or digitalis.

Unger[24] used sulfonamide drugs in the treatment of severe intractable asthma with improvement in only four of 23 cases. There was no relationship between the bronchitis, as evidenced by leucocytosis and fever, and the response to therapy. Sulfonamide blood levels were not made.

Bronchopulmonary Suppuration: Petroff and Schwartz[25] discuss the bacteriology of nontuberculous pulmonary infections; notably, lung abscess and gangrene, bronchiectasis, and pulmonary infections simulating tuberculosis or occurring in symbiosis with tuberculosis. They list the types and charac-

teristics of the many organisms generally associated with chronic pulmonary disease in a comprehensive review.

Chapman and Smith[26] have made a statistical study of the diameter of the bronchi in normal lungs and bronchiectatic lungs as shown on bronchograms. They selected three points in each lower lobe at which to measure the diameter and report on the mean sizes.

Bradshaw, Putney and Clerf[27] have made an interesting survey of the fate of patients with untreated bronchiectasis. Of 171 patients with a positive diagnosis of bronchiectasis admitted to the Jefferson Medical College Hospital between 1925 and 1935, who subsequently received no regular bronchoscopic treatment and who had no major surgical interventions, 59, or 34.5 per cent, are dead from bronchiectasis or its complications. The average duration of life in these 59 patients from the onset of symptoms to death was 13.5 years. Sixty-seven, or 39 per cent, of the series dated the onset of their pulmonary disease from what was called pneumonia, a condition the authors feel should probably better be termed pneumonitis secondary to bronchiectasis. The largest single cause of death listed for the 59 patients is pneumonia, from which 23, or 39 per cent, died.

In a symposium on bronchiectasis, Schenck[28] stresses the importance of the sinuses as an etiologic factor in bronchiectasis. He demonstrates the appearance of radiopaque media in the lung following its instillation in the sinuses, as well as evidence of iodized oil in the nasopharynx and the floor of one nasal chamber following its introduction into the trachea. Leopold[29] discusses the medical aspects of bronchiectasis and concludes that the medical treatment of bronchiectasis is effective only before the pathologic changes in the bronchi become irreversible. Pendergrass[30] in a thorough analysis of the Roentgenological consideration of the disease stresses the importance of the complete bronchography which gives the location and extent of the disease process, the structure of the bronchial tree, the condition of the flexible elements of the lung, which are discussed in detail, the degree of fixation and the time required for the lung to drain. The surgical aspects of the disease are discussed by Johnson,[31] who presents 12 patients operated for bronchiectasis, six requiring lobectomy, and six total pneumonectomy. There were no deaths, and the author points out the low mor-

tality rates of similar series reported by others in the surgical treatment of bronchiectasis. In discussing the bronchoscopic aspects of bronchiectasis, Tucker[32] presents several important considerations. He stresses the important part played by bronchial obstruction in the development of bronchiectasis and points out the manner in which bronchoscopy aids in establishing pulmonary drainage and, consequently, in preventing bronchiectasis. A preliminary report of significant experimental studies in which sulfanilamide or its derivatives were introduced by bronchoscopic insufflation is made. Tucker states that details regarding methods and dosage will be published later. Further experimental and clinical research on this latter subject is published elsewhere.[33,34]

In an exceedingly important and timely article, Riggins[35] discusses the etiology, pathogenesis, morbidity and mortality of bronchiectasis. He states that in a large series of cases observed at Bellevue and Lenox Hill Hospitals during the past 10 years, no proven case of congenital bronchiectasis was seen. Furthermore, in a large percentage of the cases bronchiectasis preceded evidence of sinus infection, another of the etiologic factors frequently associated with the disease. Riggins states that any condition which predisposes to, or causes the development of chronic inflammatory changes in the lung parenchyma and bronchi may lead to the development of bronchiectasis; such conditions include the bronchopneumonias of childhood, chronic inflammatory changes in the bronchial mucosa, bronchial obstruction due to foreign bodies, infected secretions, stenoses, benign tumors or tuberculosis of the bronchial wall. He stresses the importance of diagnostic bronchoscopy but feels that therapeutic bronchoscopy is of doubtful value except in patients having foreign bodies, benign bronchial tumors or stenoses of the stem bronchi. He stresses surgical extirpation of the diseased lobes in selected cases.

Another important survey of the natural history of bronchiectasis is given by Ogilvie[36] in one of the most comprehensive studies of the disease which has appeared in the recent literature.

Bronchiectasis need not be a widespread and diffuse disease, according to Chapman and Wiggins.[37] They present six cases of circumscribed bronchiectasis, concluding that the symptoms may be the same as in the more advanced disease but of a lesser degree.

In a series of 38 cases of bronchiectasis, Carpenter, Kerr and McMurray[38] administered from 1,500 to 1,600 r. in daily doses of 100 r. to 200 r. over three fields, anterior, lateral and posterior. This therapy was of greatest value as an adjunct in the treatment of patients who are not amenable to surgical treatment or were not able to withstand other active treatment.

Bronchiectasis is the most common suppurative condition for which operative removal of lung tissue is indicated, according to Shaw.[39] While he stresses the importance of postural drainage and bronchoscopic aspiration, he feels that because the lesion once established is irreversible, methods of therapy short of surgery will fail to provide a cure. Eight of his series of 17 lobectomies were done for bronchiectasis. Four of the patients are free of symptoms, and three greatly improved. One patient with a bilateral lesion died suddenly seven weeks after the first lobectomy, due to extensive pneumonitis of the unoperated side.

The surgical treatment of bronchiectasis is stressed by other authors as of increasing value and safety, and it should receive prominent mention in this review of bronchology.[40-47]

Lung Abscess: During the past year, lung abscess has received considerable attention in the literature of bronchology. Rodriguez[48] mentions bronchoscopy as a diagnostic and therapeutic aid in the management of 10 cases of pulmonary abscess. Ferrarini,[49] Grez,[50] Sassi,[51] and Moersch and Olsen[52] discuss the rôle of bronchoscopy in the treatment of this disease.

Postoperative Atelectasis: From an analysis of 30 cases of postoperative massive collapse of the lungs, Lell[53] concludes that etiologic factors of this disease are the aspiration of food and secretion during the operation, upper respiratory infections, unsuspected pulmonary pathology, particularly bronchiectasis, the indiscriminate use of preoperative sedatives and the too frequent and unnecessary use of intratracheal anesthesia. He includes the latter factor because of the ease with which secretions may enter the trachea when the glottis is held open by a large catheter. Unless such secretions are properly removed, Lell believes that these may precipitate atelectasis. It is of interest to note the type of oper-

ation and the anesthesia used. Nine of the 30 patients had no general anesthetic. Seven patients had thoracoplasty operations under local anesthesia, six cholecystectomies with gas-ether anesthesia, and four appendectomies under gas, ether or spinal anesthesia. In 22 of the patients, only one bronchoscopic aspiration was necessary; in four, two aspirations, and in two, three aspirations. Hyperventilation, postural drainage and limitation of sedatives are advocated, to be followed by bronchoscopic aspiration if these methods are unsuccessful. In reviewing six cases, Niemeyer[54] states that atelectasis has been established as one of the commoner postoperative complications and is due to plugging of the bronchi or bronchioles, causing lobular, lobar or multilobar involvement. A sudden elevation in temperature, associated with an increased pulse and respiratory rate in the first 24 hours following upper abdominal surgery should suggest atelectasis. Inhalation anesthesia on patients with productive processes in the lungs should be avoided according to this author's experience. Treatment consists of thinning bronchial secretions by expectorants, postural drainage, carbon dioxide, deep respirations, coughing and, if severe, bronchoscopic aspirations.

Haight and Ransom[55] agree with these measures and suggest certain prophylactic measures to prevent this complication. Postoperatively, they suggest elevation of the foot of the bed in addition to the carbon dioxide inhalations and support of the area of incision as the patient is urged to cough. For removal of tracheal and bronchial secretions, they suggest the introduction of a No. 16 French, soft rubber catheter without anesthesia, attached to suction apparatus delivering 15 to 25 pounds of suction pressure. The catheter is guided through the nose and into the trachea and the suction applied intermittently. A further discussion of the bronchoscopic therapy is given by Fisher,[56] who presents the results of therapy of nine cases.

Bronchial Tuberculosis: Allison,[57] in discussing bronchial obstruction in pulmonary tuberculosis, states that the most important cause of obstruction of the smaller bronchi is tuberculous disease of the bronchial wall through the formation of granulation tissue, scar tissue, thickened, inflamed, edematous mucous membrane, or by submucous tuberculous infiltration. Obstruction due to viscid tuberculous mucopus

may produce massive pulmonary collapse similar to that seen postoperatively, and the author feels that if this occurs in a lower lobe following a first-stage thoracoplasty for an upper lobe lesion, the patient should be treated by bronchoscopic aspiration to avoid permanent bronchial damage and bronchiectasis. Pressure from tuberculous disease outside the bronchus forms a third factor of bronchial obstruction in pulmonary tuberculosis. The commonest cause of such extrabronchial pressure is, of course, glandular, but interlobar effusion may do likewise. Allison mentions a neuromuscular component to most bronchial obstructions which simulates an asthmatic attack, and also points out that a nontuberculous lesion such as a foreign body, or bronchogenic carcinoma may sometimes obstruct a bronchus to complicate pulmonary tuberculosis.

Myerson[58] reviews the indications and contraindications for bronchoscopy in tuberculous patients resulting from experiences gained from bronchoscopies performed on 580 tuberculous patients. One hundred and sixty of these patients had bronchoscopic evidence of tuberculosis. Bronchoscopy is indicated routinely before thoracoplasty, or following it, or a pneumothorax if sputum remains positive in an apparently controlled lesion. Wheezing respiration, unexplained atelectasis, unexpected spread, or a positive sputum with negative Roentgen findings are further indications for bronchoscopy. Active laryngeal tuberculosis and recent hemoptysis are considered contraindications to the use of the bronchoscope. Myerson states that except for the granuloma secondary to a perforating mediastinal gland, the bronchial lesion is always secondary to an ulcerous lesion in the lung parenchyma and follows a definite course, the various stages of which are predictable. These consist of the submucous infiltrative stage, followed by the ulcerogranulomata and eventually by the fibrosis and stenosis associated with healing. He believes that treatment is of no value because of the nature and extent of the disease, and because the bronchial lesions heal spontaneously.

An interesting series of tuberculous esophagotracheobronchial fistulas is reported by Monserrat[59] as unusual complications of bronchial tuberculosis. Morlock,[60] Gomez,[61] Becker and Holmes,[62] Farber, [63], and Kernan and Cracovaner[64] further discuss endobronchial tuberculosis, while Oechsli[65] mentions the Roentgenographic appearance of this lesion.

Fungus Diseases of Lung: Fungus diseases of the lung are receiving increasing recognition since more thorough search of bronchoscopically obtained secretions has revealed the presence of many types of pathogenic fungi. Penta[66] emphasizes the close resemblance of this type of infection to that of pulmonary tuberculosis. It is impossible to satisfactorily review this comprehensive article at this time. He discusses the type of pathogenic fungi, their morphologic characteristics, the important clinical manifestations and the manner of establishing the diagnosis in suspicious cases. Lubchenco,[67] Hotchkiss,[68], Jamison and Hopkins,[69] Vitug and Cruz[70] and Diaz Rivera[71] discuss further this important question, and report interesting and unusual cases in which the diagnosis was aided or established by the bronchoscopically obtained specimen.

Benign Bronchial Neoplasm: Jackson and Konzelmann[72] presented the endoscopic findings and histology of this important group of bronchial tumors which is coming to be widely recognized as a clinical and pathologic entity. These tumors have some of the pathologic characteristics of low-grade carcinomas and may occasionally undergo malignant change. However, because of their cellular structure and their apparent incapacity to infiltrate or metastasize, they indicate a relatively benign character. They feel that many of the "inflammatory tumors," polyps, hemangiomas and fibromas in the literature could be classed with the adenomas pathologically and clinically. Of special interest in this report is the fact that it gives the present status of a series of 12 cases of bronchial tumors thought to be of this type reported by Jackson and Konzelmann five years ago. Three of the 12 have now been recognized as low-grade adenocarcinomas, with histologic characteristics which in retrospect distinguish them from the other nine. In discussing therapy, they stated that bronchoscopic treatment is effectual in most cases of benign adenoma and other benign bronchial tumors, but often a number of treatments are required. In some cases they find it impossible to obtain a complete and permanent cure, such as will make subsequent treatment unnecessary. In view of the definitely benign character of these tumors, and the excellent results obtained by conservative treatment, it would seem that it should be given a trial in every case, but surgical treatment of more radical character may be justifiable in some of the cases.

Goldman and Stephens,[72] and Brunn and Goldman[74] report a series of 19 cases of bronchial adenoma from their own series, and 40 additional cases personally reviewed from other clinics. They state that the accurate diagnosis of a bronchial adenoma should include more than the discovery of its mere presence. It should indicate the exact location with reference to the lobar bronchi, the presence or absence of bronchial obstruction, the size, shape and extent of the extrabronchial portion, its relations to the inner bronchial wall and, finally, the condition of the distal lung. They state that the endoscopic treatment of these tumors is less commonly indicated than it was formerly thought to be because of local recurrences, the danger of fatal complications, the inability to remove adequate amounts of the tumor, and because of the suppurating lung remaining distal to the tumor. Endoscopic removal is indicated to re-establish bronchial drainage, but the authors indicate that these patients eventually change from a problem of bronchoscopic therapy to one of pulmonary resection.

Foster-Carter[75] discusses these tumors further. Davidson[76] reports a case of primary chondroma of the bronchus.

Malignant Bronchial Neoplasms: In a 10-year survey of necropsies in the Charity Hospital at New Orleans, Halpert[77] found a relative and an absolute increase of carcinoma of the lung. In the total necropsy material there was a proportion of two males to one female. Carcinoma of the lung, however, occurred in a proportion of 10 males to one female. Of the 135 carcinomas of the lung, 74, more than 50 per cent, were squamous cell; 39, approximately 30 per cent, were reserve cell; and 22, less than 20 per cent, were columnar cell carcinomas. A comparison with the number of other carcinomas of the same series suggests that carcinoma of the lung is becoming the second if not the most common malignant neoplasm in the male. Menne and Anderson[78] likewise note the increasing incidence of bronchogenic carcinoma, 517 cases having been observed in 33,945 autopsies performed in the Pacific Northwest. In 84 cases observed by them, 78 were men, six women. Of 56 cases in which autopsy was done, 31 were squamous cell carcinomas, 13 so-called adenocarcinoma, and 12 reserve cell carcinoma.

General interest in cancer of the lung is being forced upon the profession by the established fact of its frequency. In a discussion dealing with cancer of the lung as a surgical prob-

lem, Overholt[79] stresses the importance of speeding up the mechanism of discovery of the lesion. Proper management of the patient who has either a suspected or proven cancer, accurate appraisal of the condition of the patient as to operability, and recognition of the value of surgical exploration in patients presenting presumptive evidence of cancer but in whom the diagnosis is unverified histologically are of greatest importance. A resumé of 174 patients studied clinically is given, in which 127 cases were verified histologically. Of the 127 cases, 78 cases, or 61 per cent, were diagnosed by biopsy obtained bronchoscopically; 28 cases, or 22 per cent, by biopsy from surgical exploration, 7 per cent from biopsy of metastases, 3 per cent from pleural fluid, 5 per cent at autopsy, and 2 per cent from aspiration of the tumor. It is significant to realize that of the above number, only five cases were rejected for surgery because of advanced age or too poor a general condition. It is pointed out that the question of operability is not an easy one to settle. In dealing with a disease which is 100 per cent fatal without surgical excision, the benefit of doubt must be given to every patient, especially when malignancy originating in the lung is near the top of the list as a cause of cancer death, and is curable in its early stages.

Gebauer[80] differentiates bronchogenic carcinoma clinically and pathologically into small cell carcinoma, adenocarcinoma and squamous cell carcinoma. He states that the X-ray appearance is rather characteristic of each type, especially early in the disease. The bronchoscopic picture is also somewhat characteristic, but if negative should be supplemented by other procedures until the cause for symptoms is known. The diagnostic value of early bronchoscopy is of importance to the surgeon especially when cases are still in the operable state.

The value of bronchoscopy as an aid in the diagnosis of bronchogenic carcinoma is accepted in the surgical as well as the endoscopic literature of this disease. The thorough comprehensive discussion of the subject as a whole by Oschner and DeBakey[81] stresses the importance of the diagnostic bronchoscopy. Betts,[82] Cracovaner,[83] Harrington and Moersch,[84] and Moore[85] discuss the actual bronchoscopic aspects more in detail.

Cabitt[86] discusses the relation between hemothorax and primary carcinoma of the lung in 86 cases of hemothorax. Thir-

ty-five, or 41 per cent, were due to bronchogenic carcinoma. The age, symptoms, signs, X-rays and site of the lung lesion in these patients are presented, and the value of bronchoscopy in hemothorax without cancer cells is stressed. The uncommon association of metastatic pulmonary neoplasm with hemothorax is mentioned. Neubuerger[87] reports a case of primary multiple alveolar cell tumor of the lung in which the clinical findings and the characteristic X-ray picture are shown and the origin of the tumor cells traced from the septal cells of the alveolar walls. The relation between this type of tumor and other conditions showing formation of alveolar lining in both men and animals is illustrated.

Holinger and Rigby[88] present three cases of bronchogenic carcinoma which gradually infiltrated both lungs to produce death without evidence of bronchial obstruction or pulmonary suppuration. The cases were characterized clinically by a nonproductive cough and X-ray evidence of an extensive bilateral infiltrative process similar to that produced by fungus disease. In each case a small, silent bronchogenic carcinoma spread by an invasion of the peribronchial and perivascular lymphatics without erosion of the bronchial walls. In none of the three cases was distant metastases of significance. Thus, the recognized criteria in the symptomatology, Roentgen examination and bronchoscopic appearance generally used in establishing the diagnosis of bronchogenic carcinoma were absent in the cases presented.

Cotton[89] points out that peripheral primary cancer of the lung and solitary pulmonary metastases offer some difficulties in differentiation. Due to the fact that both types may be peripheral and thus beyond bronchoscopic range, histological proof is frequently unobtainable. In such instances, methods other than bronchoscopy must be utilized to obtain tumor cells for verification of the diagnosis. The author stresses the importance of exploratory thoracotomy as the procedure of choice and illustrates the manner in which this procedure settled doubtful diagnoses in two cases and led to pneumonectomies that promise to be curative. Tenzel[90] classifies the tumors histologically as epidermoid, adenocarcinoma and anaplastic carcinoma. It is important to note that in a series of 192 patients with primary carcinoma of the lung who were examined postmortem, one-third of the 102 patients with epidermoid carcinoma had no distant metas-

tases, while in 92 per cent of the adenocarcinomas (50 cases) and anaplastic carcinomas (37 cases), distant metastases were found. Radiation therapy for primary carcinoma of the lung has its usefulness in palliation and in prolonging life, according to the report of Tenzel. Symptomatic relief was obtained by 45 per cent of the patients treated in this manner, and the survival of the irradiated patients was on an average five months longer than that of the patients not so treated.

THE ESOPHAGUS.

The value of esophagoscopy in the diagnosis and treatment of esophageal disease is discussed comprehensively by Martin[91] and by Haslinger.[92] The frequent association of esophageal symptoms with neuroses of one type or another has long been a barrier to the early diagnosis of organic lesions. However, according to Beatty and Palmer,[93] true esophageal neuroses do exist in a group of patients exhibiting functional difficulties in swallowing certain kinds of food or medication. These patients are not all of a typical neurotic type, have no structural change or history of trauma, and have no spasm of the upper or lower ends of the esophagus. The authors stressed the importance of the direct esophagoscopic examination of these patients, both for diagnosis and treatment, and suggested a very limited use of anesthesia for the procedure. It was felt that psychotherapy alone was insufficient treatment. Training in the swallowing act was considered essential. Faulkner, Rodenbaugh and O'Neill[94] were able to demonstrate the influence of the emotions upon esophageal function comparing the esophagoscopic and the Roentgen findings of esophageal spasm and dysfunction produced by certain emotions. They found objective psychosomatic changes in 25 patients, consisting of fleeting, transient spasms or even cardiospasm that could be induced or made to disappear in response to suggestion. They emphasized that these transient spasms are significant in spite of the fact that most Roentgenologists do not include them in their reports. They also felt that these "suggested" spasms may be forerunners of more permanent "habit spasms" if left unattended. An additional paper by Faulkner[95] further discussed the esophagoscopic appearance of these spasms.

Organic lesions of the distal esophagus have received considerable attention in the literature of the year. Browne and

McHardy[96] in a discussion of the medical management of cardiospasm described a combination mercury and pneumatic dilator which is efficient in dilatations of the cardia. The use of prostigmin in megoesophagus was advocated by Meyer and Necheles,[97] who found the tonus and peristaltic rate of the esophagus in two patients had increased following its administration. Gilbert[98] discussed hiatal hernia of the esophagus, showing the manner in which the history and symptomatology lead to the diagnosis. He emphasized the medical management of these cases. Shutkin[99] described this type of case further and classified the group according to the symptomatology. Such a classification has an obvious disadvantage in that the obstructive, dyspeptic and cardiac group of symptoms frequently occur in the same patient. The author mentions phrenectomy in discussing the surgical management of these cases. Polley[100] reports the findings in a series of 47 patients with congenitally short esophagus with thoracic stomach and esophageal hiatus hernia.

Mosher[101] states that the esophagus is subject to acute and chronic infection, not only from within but also from without as the result of systemic disease. Three cases are reviewed, showing narrowing at the cardia in newborns, best explained by fibrosis due to antenatal infection rather than spasm. The chief sources of infection in the lower end of the esophagus are diseases of the liver and gall bladder and of the appendix. Periesophageal abscess, from whatever cause, is not uncommon at the cardia. Dilatation of superficial veins with resulting hemorrhages exposing the subepithelial tissues and forming an ulcer may also result in obstruction due to fibrosis. Infection followed by this fibrosis is a logical, proven and a common cause of stricture of the esophagus.

According to Johnson,[102] 70 per cent of the cases of esophageal strictures he has observed are due to the ingestion of lye. He discusses the various types of therapy which may be employed, favoring gastrostomy and Tucker retrograde dilatation. When a string cannot be swallowed, he follows the method suggested by Iglauer: guidance of a filiform bougie or catheter through the cardia and along the esophagus by means of a cystoscope introduced into the stomach. Camiel and Loewe[103] mention a seldom recognized pulmonary complication of esophageal stenosis, aspiration pneumonia, which must be guarded against in these patients. Three cases

of cicatricial stricture of the esophagus following intubation are reported by Vinson,[104] who stressed the importance of vomiting as a factor responsible for the ulceration and stenosis.

The treatment of esophageal varices by the injection of sclerosing solutions introduced through the esophagoscope has received increasing attention during the past year. In a comprehensive discussion of the subject, Moersch[105,106] described the technique of the procedure and the results that were obtained in the treatment of 11 patients. An esophagoscope with both proximal and distal illumination was used to expose the varices. Five to 7 cc. of a 2.5 to 5 per cent solution of sodium morrhuate were injected into the varix through a long, specially constructed needle. Six of the patients had had splenectomies, but massive hemorrhages had continued. Three to 14 injections were given these patients and the number of hemorrhages was markedly reduced. While the author stated that in all cases the number and severity of the hemorrhages had been reduced, and that the general health of the patients as a group had improved considerably, sufficient time had not yet elapsed to draw definite conclusions as to the efficacy of the procedure.

From a review of the literature pertaining, that the *Bronchoesophagology* published during 1941, it would appear that the most significant trend is the increase in the indications for surgery of the esophagus. Gray and Sharp,[107] Mitchell[108] and Carter[117] discuss benign lesions at the lower end of the esophagus, stressing the surgical aspects of cardiospasm, epiphrenal diverticula, atresia, strictures, and benign tumors, in addition to their medical and esophagoscopic aspects. Recent progress in the surgical treatment of carcinoma of the esophagus has been of even greater importance. Benedict,[109] Ayala González,[110] Ferrari,[111] Johnson,[112], Adams,[113,114] Ochsner and DeBakey,[115] Phemister[116] and many others have described extensive work in experimental surgery in this area. They have described operative technique, established indications and contraindications for surgery, and have presented series of operated cases. While these series are for the most part still small, they demonstrated the value of early diagnosis by esophagoscopy in patients with dysphagia but negative Roentgen examinations of the esophagus. Thus, the work of these authors shows great progress in the treatment of a condition which has in the past been associated with an almost hopeless

prognosis. As an example, of cases operated by Garlock,[118] the average patient with carcinoma of the middle third of the esophagus stands a 54 per cent chance of surviving operation and a 30 per cent chance of living more than one year. The patient with squamous cell carcinoma of the lower third stands a 70 per cent chance of surviving operation and a 100 per cent chance of living two years. With adenocarcinoma of the cardia, a 60 per cent chance at operation and an 80 per cent chance of living one year.

Costen and Bryan[119] review various phases of the diagnosis of carcinoma of the esophagus from symptomatologic, Roentgenologic and esophagoscopic standpoints. They present the findings in 106 cases of carcinoma of the esophagus. Lindsay[120] states that the earliest symptoms of progressive discomfort or difficulty in swallowing are indications for thorough X-ray studies and esophagoscopy. This is imperative and should be done early so that surgical removal of carcinoma of the esophagus will result in more cures, especially since this disease accounts now for from 2 to 8 per cent of all tumor deaths. Hagens[121] reports eight cases of cancer of the esophagus and discusses some of the difficulties in the diagnostic esophagoscopic procedure. The firm border of fixed edematous tissue proximal to the lesion itself, the narrow field of vision at times which prevents getting to the tumor, and the risk of perforation due to the thinning out of the lumen caused by the tumor are mentioned. The author states that because of these difficulties ample time should be given the endoscopist so that an intelligent esophageal examination may be carried out.

Perforations of the esophagus due to foreign bodies are reported[122] and the complications of esophageal perforation discussed.[123]

Gastroscopy: The extensive literature of gastroscopy cannot be reviewed in this paper except as it pertains to foreign bodies. In an editorial, Bunch[124] stressed the value of X-rays in locating ingested foreign bodies and stated that in general the treatment is watchful expectancy, and that laxatives should never be given. He lists the symptoms of perforation and discusses the surgical management. Chatterjee and Maitra[125] present unusual aspects of ingested foreign bodies swallowed, either to elude detection in thievery or as acts of professional jugglers. In one of their cases several hundred nails and other objects were removed from the stomach.

In another case, nails and glass weighing 2 pounds 8 ounces had been ingested.

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